PI: **Heinemann, Allen Walter**	Title: Defining Trajectories of Linguistic, Cognitive-Communicative and Quality of Life Outcomes in Aphasia	
Received: 07/05/2018	FOA: PA18-287 Clinical Trial:Optional	Council: 01/2019
Competition ID: FORMS-E	FOA Title: Improving Outcomes for Disorders of Human Communication (R01 Clinical Trial Optional)	
1 R01 DC017174-01A1	Dual:	Accession Number: 4194643
IPF: 6898901	Organization: REHABILITATION INSTITUTE OF CHICAGO D/B/A SHIRLEY RYAN ABILITYLAB	
Former Number:	Department:	
IRG/SRG: LCOM	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: [redacted] Year 2: [redacted] Year 3: [redacted] Year 4: [redacted] Year 5: [redacted]	Animals: N Humans: Y Clinical Trial: N Current HS Code: 30 HESC: N	New Investigator: N Early Stage Investigator: N
Senior/Key Personnel:	*Organization:*	*Role Category:*
Allen Heinemann Ph.D	Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab	PD/PI
Leora Cherney Ph.D	Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab	MPI
Andrea Domenighetti	Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab	Co-Investigator
Marwan Baliki	Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab	Co-Investigator
Elliot Roth	Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab	Co-Investigator
Linda Foster	Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab	Co-Investigator
Allan Kozlowski Ph.D	Mary Free Bed Rehabilitation Hospital	Co-Investigator

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

3. DATE RECEIVED BY STATE	State Application Identifier

1. TYPE OF SUBMISSION*

● Pre-application ● Application ● Changed/Corrected Application

4.a. Federal Identifier
DC017174

b. Agency Routing Number

2. DATE SUBMITTED | **Application Identifier**

c. Previous Grants.gov Tracking Number

5. APPLICANT INFORMATION

Organizational DUNS*: [redacted]

Legal Name*: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab
Department:
Division:
Street1*: [redacted]
Street2:
City*:
County:
State*:
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*:

Person to be contacted on matters involving this application
Prefix: Mrs. First Name*: Evelyn Middle Name: Scott Last Name*: DiLisio Suffix:
Position/Title: Executive Director, Research Administration
Street1*: [redacted]
Street2:
City*:
County:
State*:
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*:
Phone Number*: Fax Number: Email [redacted]

6. EMPLOYER IDENTIFICATION NUMBER *(EIN) or (TIN)** [redacted]

7. TYPE OF APPLICANT* M: Nonprofit with 501C3 IRS Status (Other than Institution of Higher Education)

Other (Specify):
Small Business Organization Type ● Women Owned ● Socially and Economically Disadvantaged

8. TYPE OF APPLICATION*

● New ● Resubmission
● Renewal ● Continuation ● Revision

If Revision, mark appropriate box(es).
● A. Increase Award ● B. Decrease Award ● C. Increase Duration
● D. Decrease Duration ● E. Other *(specify)* :

Is this application being submitted to other agencies?* ●Yes ●No What other Agencies?

9. NAME OF FEDERAL AGENCY*
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER
TITLE:

11. DESCRIPTIVE TITLE OF APPLICANT'S PROJECT*
Defining Trajectories of Linguistic, Cognitive-Communicative and Quality of Life Outcomes in Aphasia

12. PROPOSED PROJECT
Start Date* 04/01/2019
Ending Date* 03/31/2024

13. CONGRESSIONAL DISTRICTS OF APPLICANT
[redacted]

14. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION

Prefix: Dr. First Name*: Allen Middle Name: Last Name*: Heinemann Suffix: Ph.D
Position/Title: Director
Organization Name*: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab
Department:
Division:
Street1*: [redacted]
Street2:
City*:
County:
State*:
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*:
Phone Number*: Fax Number: Email*:

15. ESTIMATED PROJECT FUNDING

a. Total Federal Funds Requested* [redacted]
b. Total Non-Federal Funds*
c. Total Federal & Non-Federal Funds*
d. Estimated Program Income*

16.IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?*

a. YES ○ THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON:
DATE:
b. NO ● PROGRAM IS NOT COVERED BY E.O. 12372; OR
○ PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

17. By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

● I agree*

** The list of certifications and assurances, or an Internet site where you may obtain this list, is contained in the announcement or agency specific instructions.*

18. SFLLL or OTHER EXPLANATORY DOCUMENTATION File Name:

19. AUTHORIZED REPRESENTATIVE

Prefix: Mrs. First Name*: [redacted] Middle Name: [redacted] Last Name*: [redacted] Suffix:
Position/Title*: Executive Director, Research Administration
Organization Name*: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab
Department:
Division:
Street1*: [redacted]
Street2:
City*:
County:
State*:
Province:
Country*: USA: UNITED STATES
ZIP / Postal Code*:
Phone Number*: Fax Number: Email*:

Signature of Authorized Representative* [redacted]

Date Signed* 07/05/2018

20. PRE-APPLICATION File Name:

21. COVER LETTER ATTACHMENT File Name:

424 R&R and PHS-398 Specific
Table Of Contents

Project/Performance Site Location(s)

Project/Performance Site Primary Location

○ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab
Duns Number: [redacted]
Street1*: [redacted]
Street2:
City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]
Project/Performance Site Congressional District*: [redacted]

Project/Performance Site Location 1

○ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: Mary Free Bed Rehabilitation Hospital
DUNS Number: [redacted]
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: [redacted]
Zip / Postal Code*: [redacted]
Project/Performance Site Congressional District*: [redacted]

Project/Performance Site Location 2

○ I am submitting an application as an individual, and not on behalf of a company, state, local or tribal government, academia, or other type of organization.

Organization Name: Northwestern University
DUNS Number: [redacted]
Street1*: [redacted]
Street2:
City*: [redacted]
County: [redacted]
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]
Project/Performance Site Congressional District*: [redacted]

Additional Location(s) File Name:

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED Other Project Information

1. Are Human Subjects Involved?* ● **Yes** ○ **No**

1.a. If YES to Human Subjects

Is the Project Exempt from Federal regulations? ○ Yes ● No

If YES, check appropriate exemption number: — 1 — 2 — 3 — 4 — 5 — 6 — 7 — 8

If NO, is the IRB review Pending? ● **Yes** ○ **No**

IRB Approval Date:

Human Subject Assurance Number 00001553

2. Are Vertebrate Animals Used?* ○ **Yes** ● **No**

2.a. If YES to Vertebrate Animals

Is the IACUC review Pending? ○ Yes ○ No

IACUC Approval Date:

Animal Welfare Assurance Number

3. Is proprietary/privileged information included in the application?* ○ **Yes** ● **No**

4.a. Does this project have an actual or potential impact - positive or negative - on the environment?* ○ **Yes** ● **No**

4.b. If yes, please explain:

4.c. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed? ○ Yes ○ No

4.d. If yes, please explain:

5. Is the research performance site designated, or eligible to be designated, as a historic place?* ○ **Yes** ● **No**

5.a. If yes, please explain:

6. Does this project involve activities outside the United States or partnership with international collaborators?* ○ **Yes** ● **No**

6.a. If yes, identify countries:

6.b. Optional Explanation:

	Filename
7. Project Summary/Abstract*	1242-Heinemann_Abstract.pdf
8. Project Narrative*	1243-Heinemann_ProjNarrative.pdf
9. Bibliography & References Cited	1244-Heinemann_Refs.pdf
10.Facilities & Other Resources	1245-Heinemann_Facilities.pdf
11.Equipment	1246-Heinemann_Equipment.pdf

Funding Opportunity Number: PA-18-287. Received Date: 2018-07-05T15:37:27.000-04:00

Stroke imposes significant burdens on the health and quality of life of survivors and their caregivers, and presents a major public health issue in terms of healthcare costs and lost productivity. Aphasia adds to the cost of stroke-related care. Many stroke survivors with aphasia receive therapy in inpatient rehabilitation facilities. However, aphasia recovery is variable and there is limited evidence on the benefits of inpatient rehabilitation on outcomes.

The objective of this study is to describe the trajectories of linguistic, cognitive-communicative, and health-related quality of life (QoL) outcomes following stroke in persons with aphasia during inpatient and outpatient rehabilitation to 18 months following stroke. A sample of 300 consecutively-admitted stroke patients with aphasia recruited at three Midwestern rehabilitation hospitals will complete measures of linguistic and cognitive-communicative performance, and the Quality of Life in Neurological Disorders (Neuro-QoL) Measurement System instruments during rehabilitation and at 6-,12-, and 18- months post-stroke. We will model outcomes as individual and group trajectories, allowing us to develop individual predictions which could inform clinical planning and decision-making for new patients. The Specific Aims are to:

Aim 1: Establish a prospective cohort of stroke patients with aphasia, and define their typical trajectory of linguistic, cognitive-communicative, and health-related QoL recovery at admission to and discharge from the IRF, and at 6, 12, and 18 months post onset.

Aim 2: Identify factors that are associated with linguistic, cognitive-communicative, and health-related QoL outcomes from among the following: patient factors including demographic and clinical characteristics related to stroke and aphasia; treatment variables including inpatient and outpatient aphasia therapy characteristics and informal aphasia services; and biomarkers, including genetic and neuroimaging biomarkers.

Aim 3: Evaluate the stability of the models of linguistic, cognitive-communicative, and health-related QoL outcomes recovery that are developed from Aims 1 and 2.

This study is innovative in its use of (1) standardized assessments that measure not only linguistic outcomes but also communication and QoL outcomes; (2) patient-centered, self-report instruments such as Neuro-QoL to detect clinically important change through 18 months post-stroke; (3) individual growth curve analysis to describe recovery trajectories and examine associations between demographic, lesion, aphasia, genetic, and speech and language therapy characteristics; (4) biomarkers that have been implicated in promoting neuroplasticity; (5) resting state functional magnetic resonance imaging to evaluate the association between network pathology and recovery from aphasia; (6) information on type, amount, and duration of aphasia treatment provided in clinical settings; and (7) information on informal aphasia services following discharge from formal therapy.

Project Narrative

This study describes trajectories of linguistic, cognitive-communicative, and health-related QoL outcomes during inpatient and outpatient rehabilitation to 18 months in a sample of 300 adults with aphasia using demographic, lesion, aphasia, genetic polymorphisms, and speech and language therapy characteristics as predictors.

Facilities

The Shirley Ryan AbilityLab (formerly the Rehabilitation Institute of Chicago)

The Shirley Ryan AbilityLab (SRALab) is an internationally recognized specialty hospital and healthcare network dedicated to the care and rehabilitation of individuals with physical disabilities. Recognized by *U.S. News and World Report* as the number one rehabilitation provider for 27 consecutive years, SRALab has been a leading center for over 60 years. SRALab shares facilities and teaching staff with the NU-McGaw Medical Center and affiliated hospitals. The Department of PM&R of NU's Feinberg School of Medicine, is housed at SRALab, which has 42-attending PM&R physicians, and 151 consulting physician specialists. The Joint Commission accredits AbilityLab.

Clinical Services: The SRALab opened in March 2017 two blocks south of the old RIC flagship hospital. It is expanded significantly from the old RIC, with 27 floors, 1.2 million square feet, with 242 all private, inpatient beds. Last year, the organization served approximately 58,000 patients from 43 states and 64 countries. The SRALab infuses biomedical science and research into the clinical environment. Traditional therapy gyms are replaced with Ability Labs. Within each Lab clinicians, researchers, and patients collaborate in open space and real time. The Labs are organized by functional outcome rather than by diagnosis and include: *Think & Speak* (Speech & Cognition); *Arms & Hand* (Fine Motor); *Legs & Walking* (Gait and Locomotion); *Strength & Endurance* (Total Body); and *Pediatrics*. The clinical staff includes Physical Therapy, Occupational Therapy, Speech Language Pathology, Neuropsychology, Therapeutic Recreation, Rehabilitation Nursing, Case Management, a Behavioral Specialist, Family Counselors and Vocational Rehabilitation Counselors. Admission decisions are based on need for medical and rehabilitation services, and not on ability to pay. This policy ensures accessibility for all people who need these services.

Specialized services available at AbilityLab that are not available at many rehabilitation hospitals include the Technology Center, the ExpertEval™ Second Opinion Program, Brain Injury Circle of Caring Program, the AMiCous Program (Disorder of Consciousness program), TBI Global Patient Services Program, eight Day Rehabilitation Programs, Vision Clinic, Spasticity Clinic, Mild TBI Clinic, Vocational Rehabilitation Services, The Wirtz Sports Program and Galvin Center for Health and Fitness, and the LIFE (Learning, Innovation, Family, Empowerment) Center and website (https://www.sralab.org/lifecenter).

SRALab provides comprehensive rehabilitative care to a wide range of persons with disabilities in in- and outpatient settings. More than 40% of admissions come from minority backgrounds. Medicare covers about 40% of inpatient admissions, while 35% are funded by managed care insurers and 25% by Medicaid. This population provides clinicians with opportunities to evaluate the feasibility and utility of standardized assessments.

Stroke Rehabilitation Program: Stroke constitutes the largest diagnosis of patients admitted for inpatient rehabilitation care at RIC. In fiscal year 2016, SRALab admitted 522 inpatients with a primary diagnosis of stroke. Inpatients receive comprehensive and intensive rehabilitation services from an interdisciplinary rehabilitation team. The program is unique in focusing on high intensity of training.

Communication Disorders: Currently, within the SRALab's main building, Communication Disorders services are provided to an estimated 900 patients with neurogenic communication disorders per year. In addition, there are eight community based Day-Rehabilitation Programs which are strategically located to serve a large geographic region of the greater Chicago area. Two Day-Rehabilitation programs are located in the City; the others are located in suburban areas. For example, one is approximately 20 miles north of the city in Northbrook, while another is located approximately 20 miles south west of the city in Willowbrook. Having multiple locations allows access to a larger number of potential subjects for research activities.

As of June 2018, there were 101 licensed speech-language pathologist across the continnum of care. This includes 25 inpatient SLPs, 26 DayRehab SLPs, 10 outpatient SLPs, 21 flex staff, 3 Tech Center SLPs, 5 research SLPs, and 11 SLPs in leadership positions. In a recent survey, 68 of 73 (93%) clinical SLPs indicated that they work routinely with patients with aphasia. Of these 68 SLPs, 33% reported having more than 10 years experience and 25% reported 5-10 years of experience.

Co-PI Cherney has an *Aphasia Research Lab* in the Think and Speak Lab located on the 25th floor of SRALab. The Lab has 1300 square feet of space, including six private offices for treating patients and/or research subjects as well as 12 carrels in open space for research staff, graduate students and post-doctoral fellows. The Aphasia Research Lab has 10 desktop PC's that are dedicated to research activities in general and 12 laptop computers that are dedicated to specific research projects. A separate computer lab with four terminals is dedicated to research participants.

Center for Rehabilitation Outcomes Research (CROR). Co-PI Heinemann is PI of projects funded by the Department of Defense, PCORI, NIDILRR, and the Craig H. Neilsen Foundation. He directs the Center for Rehabilitation Outcome Research (CROR), a rehabilitation-focused health services research program. Staff members include four doctoral-level scientists, a project manager, two project coordinators, a data analyst, and six research assistants. Under Dr. Heinemann's leadership, CROR has gained recognition for outcome studies and measurement of various disability domains. CROR manages the Rehabilitation Measures Database, an on-line compendium of measures, clinician observed instruments, and patient-reported outcome tools. Dr. Heinemann is Co-PI of AbilityLab's SCI Model Systems project. He has been involved in numerous other collaborative projects such as development of the PROMIS, Neuro-QoL, SCI-QoL, and TBI-QoL.

Imaging Facilities. Resting State fMRI scans will be acquired at the SRALab. The imaging floor at the SRALab houses a Siemens Prisma 3T whole-body MRI scanner. This is equipped with Siemens 64- and 20-channel head-neck coils as well as a Tx/Rx CP head coil. The scanner performs basic and clinical research including EPI, higher-order shimming, CINE, MR angiography, and spectroscopy. The Prisma hardware has 128 independent whole-body channels with a two-channel transmit system, a 60 cm bore, and an industry-leading XR gradient coil capable of imaging at 80mT/m with slew rates in excess of 200 T/m/s, per axis, at a duty cycle of 100% simultaneously on all axes. The scanner relies on the SRALAB imaging/radiology floor infrastructure, which is staffed with two MRI technologists, research nurses, research managers and an administrative assistant. The MRI suite contains MRI-compatible audio, visual, and somatosensory stimulation equipment as well as eye-tracking and behavioral response devices.

Biologics Lab. The Biologics Lab comprises approximately 5,000 square feet of dedicated and fully equipped laboratory space on the 26th floor of SRALab; staff will perform the genetic experiments proposed in this application. The space is set up to allow execution of many tissue, cellular, and molecular techniques including: metabolic measurements, histology, immunohistochemistry, immunocytochemistry, cell and tissue handling and cryopreservation, proteins and DNA extraction and analysis, microbiology, phase contrast, confocal and fluorescence imaging, muscle fibers and muscle bundles biomechanics, FACS sorting and cell culture. Dr. Domenighetti's group has dedicated office space on the same floor. Offices are fully equipped with computers for writing and data analysis (e.g., MATLAB, SPIKE2, SPSS, SIGMAPLOT, SAS, Adobe software and Microsoft Office), as well as printers, a scanner, fax machine and access to Northwestern University library and internet networks.

Research infrastructure: SRALab has a full complement of staff available with experience in research administration, including a Director of Grants Administration who functions as the administrative official for the institution, business support managers, a grants financial analyst, and administrative support staff. Research Administration facilitates and tracks submission of human subject research in conjunction with Northwestern University's Institutional Review Board, and several faculty members in the Department of Physical Medicine and Rehabilitation serve on the review panels. Research Administration works with the Institute's Finance and Accounting offices and with the General Counsel's office in establishing and tracking research accounts, establishing contractual agreements, invoicing, financial agency reporting, and development of Research Policies and Procedures. The Searle Rehabilitation Research Center of the SRALab has extensive experience in managing large, grant-supported research programs. Our extramural research portfolio exceeds $20 million with over 300 active projects. The Center employs over 180 individuals.

Alexian Brothers Rehabilitation Hospital

The Alexian Brothers Rehabilitation Hospital (ABRH) offers comprehensive inpatient services, day rehabilitation, outpatient services, specialty programs and on-site physician services. ABRH is a partnership between AMITA Health and the Shirley Ryan AbilityLab, offering convenient access to the same expert care that has earned SRALab the ranking of "Best Rehabilitation Hospital in America" by U.S. News & World Report every year since 1991.

Clinical Services: ABRH has 72 inpatient rehabilitation beds, as well as an intensive, interdisciplinary Day Rehabilitation program that treats patients with stroke and other neurological disorders. During FY 2016, ABRH admitted 340 patients with a primary diagnosis of stroke. Inpatient treatment includes services from board-certified physiatrists, as well as physical, occupational, and speech therapy. ABRH also has several specialized programs, including Women's Health Rehabilitation, and Vestibular/Balance Rehabilitation with state-of-the-art balance testing equipment. The NeuroCom Smart Equitest aids therapists in their evaluation and treatment of individuals with neurological impairments that result in balance deficits. The KineAssist robotic device is also used for the treatment of individuals with neurological impairments that result in balance and gait deficits. There

are 16 speech-language pathologists who provide services in inpatient, outpatient and day rehabilitation programs. ABRH also offers a community Conversation Support Group that provides people with aphasia and apraxia of speech the opportunity to practice their conversational skills with others who experience similar difficulties. The group meets weekly with approximately 20 people coming throughout the year and an average of 8 people attending each week. The group has a wide age range of attendees from their 20s to 80s. The group serves a wide range of impairment levels from mild to moderate-severe.

Research Infrastructure: AMITA Health is committed to advancing medicine by developing new ways to treat disease through research studies and clinical trials. AMITA Health is engaged in over 120 clinical trials, offered through the Behavioral Health Hospital, the Neurosciences Institute, the Heart and Vascular Institute, and the Cancer Institute. AMITA Health provides administrative support of research activities throughout the health system through its Office of Clinical Research, which has formed an Institutional Review Board to oversee ethical aspects of research.

Mary Free Bed Rehabilitation Hospital

Mary Free Bed (MFB) Rehabilitation Hospital is the main campus for a regional network and continuum of post-acute care services that extends across the lower peninsula of the state of Michigan. It is accredited by the Joint Commission.

Clinical Services: MFB operates a 119-bed inpatient rehabilitation facility which admits more than 300 persons for stroke rehabilitation annually. The MFB campus also hosts a 48-bed subacute rehabilitation unit, and adult and pediatric outpatient programs.

There are 61 credentialed speech-language pathologists (SLPs) employed across the MFB Network, who have been licensed with the American Speech-Language-Hearing Association for an average of 8.5 years. Of these, 37 are employed at the main campus: 18 Inpatient, 9 Outpatient, 2 Cover/Float, and 8 Weekend. Of the inpatient SLPs, 88% (16/18) SLPs report treating patients with aphasia, with a median 96.5% rating of comfort in treating patients with aphasia. Of the 16 inpatient SLPs who treat aphasia, 50% report more than 10 years of experience, and 37.5% report experience ranging from 5 -10 years.

Research Infrastructure: The MFB Research and Innovation Center is led by Director of Research John F. Butzer, MD. The Department was organized in 2014, and has since secured nearly a million dollars in external funding through donations, federal, and private foundation research grants. Allan J. Kozlowski, PhD joined the department in 2016 and serves as the Director of Outcomes Research. Additional staff include a Clinical Research Project Manager, a Research PT, and Research Assistants, who are funded in part by extramural grants and Department funds. A healthcare research consultant has been retained to aid in program development and growth. Research and Innovation receives technical and analytical support from MFB Departments of Information Technology and Decision Support. Mary Free Bed has a robust enterprise data warehouse to house electronic health record data. The Research and Innovation office suite includes eight private and semi-private offices, work space for post-doctoral fellows, students, and interns, and a conference room. Computer workstations are available for all department members, with software support from Mary Free Bed and from Michigan State University. All Department personnel are equipped with a laptop and docking station with complete Microsoft Office software, access to the MFB enterprise data warehouse, and other packages required for individuals. Dr. Kozlowski's laptop is equipped with SAS, R, and HLM-7 software required for the basic and advanced statistics described in this proposal. Research and Innovation personnel have access to a complete online medical library through Michigan State University.

The MFB Information Technology and Decision Support Departments work cooperatively to manage respectively the information infrastructure, data storage, and security; and data management and processing. Defined data from the MFB e medical record platforms (Cerner, Athena), scheduling, and financial systems are exported to the enterprise data warehouse daily. MFB Network providers will also contribute as data sharing agreements are established. The plan is to have data from all post-acute care encounters for MFB Network patients captured in the enterprise data warehouse and linked by a common universal patient ID number. The Information Technology Department also hosts the MFB REDCap platform, which is used for all Research Department studies, and some administrative and clinical applications that cannot be built into the EMR or other systems. The Decision Support Department manages data processing issues, and has implemented the Tableau© reporting platform as the interface between the EDW and the personnel who need information.

The Shirley Ryan AbilityLab (formerly the Rehabilitation Institute of Chicago)

Imaging Equipment. The imaging floor at the SRALab houses a Siemens Prisma 3T whole-body MRI scanner. The imaging suite is equipped with Siemens 64- and 20-channel head-neck coils as well as a Tx/Rx CP head coil. The scanner performs basic and clinical research including EPI, higher-order shimming, CINE, MR angiography, and spectroscopy. The Prisma hardware has 128 independent whole-body channels with a two-channel transmit system, a 60 cm bore, and an industry-leading XR gradient coil capable of imaging at 80mT/m with slew rates in excess of 200 T/m/s, per axis, at a duty cycle of 100% simultaneously on all axes. The MRI suite contains MRI-compatible audio, visual, and somatosensory stimulation equipment as well as eye-tracking and behavioral response devices.

Biologics Lab. The Biologics Lab is equipped with chemical fume hood, and biological safety cabinets and equipment to perform research on tissue or cell culture experiments. Offices are fully equipped with computers for writing and data analysis (e.g., MATLAB, SPIKE2, SPSS, SIGMAPLOT, SAS, Adobe software and Microsoft Office), as well as printers, a scanner, fax machine and access to Northwestern University's Galter Health Sciences library and internet networks. Specific equipment includes:

Biochemistry, molecular biology and general equipment:

- Temperature regulated water bath
- Shaker incubator (New Brunswick Scientific Excella E24)
- 96-well microplate reader (Synergy HTX)
- PCR Thermal cyclers (Bio-Rad T100)
- Real-Time PCR (Bio-Rad CFX96)
- UPLC System (Shimadzu Prominence HPLC with RF-20 and UV Detectors)
- Gel imaging equipment (Syngene PXi)
- UVP UV/While Transilluminator (analytikjena)
- pH Meter (Mettler Toledo)
- Refrigerated and regular centrifuges (2x Eppendorf 5810R, 2x Eppendorf 5424R, Eppendorf 5427R, 2x Eppendorf 5414D, 3x Eppendorf 5702R)
- SDS-PAGE and agarose gel electrophoresis equipment (Bio-Rad and Life Technologies)
- Tissue homogenizer (Bullet Blender 24)
- Digital Microbalance (Shimadzu)
- Top loader Balance (Sartorius)
- -80 ^{0}C ultra low freezers (4x New Brunswick U725)
- Standard refrigerators/freezers (7 units, ThermoScientific)
- General bench and table-top laboratory equipment (Pipettes, micro-centrifuges, plate heaters, water baths, stirrers, vortexers, drybath, thermomixer, etc.)
- Flasks Scrubber Dishwasher (Steris Reliance 400XLS)
- Autoclaving system (2x Steris AMSCO 250LS)
- Water Purification System (Elga)

Histology, immunohistochemistry and microscopy:

- Leica RM 2155 automatic microtome
- 2x Leica CM3050S cryostats with a disposable blade holder and knife holder
- Leica DM6000 B phase contrast microscope package
- Epifluorescence Leica DMi8 inverted microscope with life-cell imagining capability
- Confocal Leica DMi8 inverted microscope

Cell culture:

- 5x Tissue culture hoods (ThermoScientific 1300 Series A2)
- 6x CO_2/O_2 incubators (Panasonic)
- Liquid nitrogen containers for cell storage (Thermo Scientific Locator 4 Plus)
- Leica DMi1 microscopes for cell visualizations
- Refrigerated centrifuge (Eppendorf 5810R)
- Standard refrigerator/freezer (Thermo Scientific)

- EVE automatic cell counter
- xCELLigence RTCA DP Instrument (ACEA)
- FACS cell sorter FaxMelody (BD)
- Maestro Pro excitable cells analyzer (Axion BioSystems)

Additional equipment:

- Muscle lever system, Model 305B 305B
- Balance, Mettler PC440
- Muscle lever system, Model 360B 360B
- Microscope, MZ FLIII fluorescent dissecting MZFLIII
- Centrifuge, Eppendorf desktop 5415D
- Force transducer, Aurora Scientific 405A
- Centrifuge, Tabletop Spectrafuge 16M
- Balance, Mettler AE50 AE50
- Muscle lever system, Model 300B 300B
- Centrifuge, mini C-1200
- Power supply, electrophoresis PowerPac 200
- UV transilluminator LM-20E
- Microscope, Leica MZ12.5 dissecting MZ12
- Stimulator, Pulsar 6bp 6bp
- Microscope, MZ16 Stereomicroscope MZ16
- Transmitted light base, microscope n/a
- 2x Fiber optic light source, Schott KL1500
- Centrifuge, Eppendorf desktop 5415D
- Centrifuge, mini
- 2x Vortexers
- Muscle lever system, Model 300C-LR 300C-LR
- Aurora High-Speed length controller 318B
- Microscope, Nikon microphot-SA
- Sony camera control unit DXC-760MD
- Patch-clamp setup
- 2x muscle fiber and muscle bundle biomechanics setups.

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix: Dr. First Name*: Allen Middle Name Last Name*: Heinemann Suffix: Ph.D

Position/Title*: Director
Organization Name*: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab
Department:
Division:
Street1*: [redacted]
Street2:
City*:
County:
State*:
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number:

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: PD/PI Other Project Role Category:

Degree Type: Ph.D Degree Year: 1982

Attach Biographical Sketch*: File Name: 1235-Heinemann_Bio.pdf

Attach Current & Pending Support: File Name:

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Leora Middle Name R. Last Name*: Cherney Suffix: Ph.D

Position/Title*: Scientific Chair, Think & Speak Lab, SRALAB
Organization Name*: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab
Department:
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number:

E-Mail*: [redacted]

Credential, e.g., agency login [redacted]

Project Role*: PD/PI Other Project Role Category:

Degree Type: Ph.D Degree Year: 1990

Attach Biographical Sketch*: File Name: 1236-Cherney.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Andrea Middle Name Last Name*: Domenighetti Suffix:

Position/Title*: Research Scientist
Organization Name*: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab
Department:
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number:

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: Ph.D Degree Year: [redacted]

Attach Biographical Sketch*: File Name: 1237-Domenighetti_Bio.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Marwan Middle Name N. Last Name*: Baliki Suffix:

Position/Title*: Research Scientist
Organization Name*: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab
Department:
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number:

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: Ph.D Degree Year: 2009

Attach Biographical Sketch*: File Name: 1238-Baliki_Bio.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Elliot Middle Name J. Last Name*: Roth Suffix:

Position/Title*: Co-Medical Director
Organization Name*: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab
Department: Brian Innovation Center
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number:

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: M.D. Degree Year: 1982

Attach Biographical Sketch*: File Name: 1239-Roth_Bio.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: First Name*: Linda Middle Name W. Last Name*: Foster Suffix:

Position /Title*: Research Coordinator
Organization Name*: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab
Department:
Division:
Street1*: [redacted]
Street2:
City*: [redacted]
County:
State*:
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number:

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: M.S Degree Year: 1987

Attach Biographical Sketch*: File Name: 1240-Foster_Bio.pdf

Attach Current & Pending Support: File Name:

PROFILE - Senior/Key Person

Prefix: Dr. First Name*: Allan Middle Name J. Last Name*: Kozlowski Suffix: Ph.D

Position/Title*: Assistant Professor
Organization Name*: Mary Free Bed Rehabilitation Hospital
Department: [redacted]
Division:
Street1*:
Street2:
City*: [redacted]
County:
State*: [redacted]
Province:
Country*: USA: UNITED STATES
Zip / Postal Code*: [redacted]

Phone Number*: [redacted] Fax Number:

E-Mail*: [redacted]

Credential, e.g., agency login: [redacted]

Project Role*: Co-Investigator Other Project Role Category:

Degree Type: Ph.D Degree Year: 2010

Attach Biographical Sketch*: File Name: 1241-Kozlowski_Bio.pdf

Attach Current & Pending Support: File Name:

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.

Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Allen W. Heinemann, Ph.D.

eRA COMMONS USER NAME: [redacted]

POSITION TITLE: Professor, Physical Medicine and Rehabilitation, Feinberg School of Medicine, Northwestern University
Director, Center for Rehabilitation Outcomes Research, Shirley Ryan AbilityLab (formerly the Rehabilitation Institute of Chicago)

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Washington State University, Pullman, WA	BS	05/1977	Psychology
University of Kansas, Lawrence, KS	MA	05/1980	Psychology
University of Kansas, Lawrence, KS	PhD	08/1982	Psychology

A. Personal Statement

As Director of the Center for Rehabilitation Outcomes Research at the Shirley Ryan AbilityLab (formerly the Rehabilitation Institute of Chicago), I have the requisite expertise and experience to serve as co-PI of this application. Since 1985, I have led the AbilityLab's Center for Rehabilitation Outcomes Research, a health services research program with a focus on outcomes measurement. Our work included the original Rasch analysis of the Functional Independence Measure that demonstrated it is comprised of reliable subscores of motor and cognitive function. Other outcomes measurement-related funded projects led to the development of the Quality of Life in Neurological Disorders (NeuroQoL) measurement system, the TBI Quality of Life Measurement System, the Orthotics Prosthetics User Survey, the Patient-Reported Outcome Measurement System (PROMIS), the Spinal Cord Injury Functional Index (SCI-FI), and the Substance Abuse for Vocational Rehabilitation Screener (SAVRS), among others. I collaborated with Dr. Cherney on aphasia-related projects that generated three publications. I serve as co-PI of the Midwest Regional SCI Model System and served as co-I of the Midwest Regional TBI Model System from 2008-12; I consult with the currently-funded TBI Model Systems' Global Outcome Measures Module. I provide leadership for Northwestern University's integrated post-doctoral fellowship program in Health Services and Outcomes Research. Our most recent RRTC led to the development of the *Rehabilitation Measures Database,* an on-line compendium of systematic reviews of outcome instruments that are suitable for research and clinical applications. My research interests focus on health services research, psychosocial aspects of rehabilitation including substance abuse, and measurement issues in rehabilitation. The peer-reviewed publications to which I contributed were the result of funding from NIH, NIDILRR, (RRTCs on rehabilitation outcome measurement, DRRP on health services research, ARRT), the Patient-Centered Outcomes Research Institute, Centers for Disease Control, the Social Security Administration, the Substance Abuse and Mental Health Services Administration, among others. I have been elected a fellow of the American Congress of Rehabilitation Medicine and the American Psychological Association (Division 22). As co-Editor-in-Chief for the *Archives of Physical Medicine and Rehabilitation*, I have a unique opportunity to evaluate and provide leadership on this multisite study of aphasia recovery.

Per Scopus, my 337 publications have generated 8,347 citations and an h-index of 47 (June 22, 2018).

B. Positions and Honors

Positions and Employment

1982-1985 Assistant Professor, Psychology, Illinois Institute of Technology, Chicago IL
1985-1987 Assistant Professor, PM&R, Northwestern University Feinberg School of Medicine, Chicago IL
1985-1988 Assistant Director, Center for Rehabilitation Outcomes Research, RIC, Chicago, IL
1988-1996 Associate Professor, PM&R, Northwestern University Feinberg School of Medicine, Chicago IL
1988-present Director, Center for Rehabilitation Outcomes Research, RIC, Chicago, IL
1996-present Professor, PM&R, Northwestern University Feinberg School of Medicine, Chicago IL
1996-present Senior Faculty Fellow, Center for Healthcare Studies, Northwestern University Feinberg School of Medicine, Chicago IL
1996-present Associate Director of Research, Rehabilitation Institute of Chicago, Chicago, IL

Other Experience and Professional Memberships

1999-2004	Behavioral Medicine: Interventions and Outcomes study section member, NIH, Center for Scientific Review, Department of Health and Human Services
2003- 2007	Member, Function, Integration and Rehabilitation Sciences Subcommittee, National Institute of Child Health and Human Development Initial Review Group, NICHD
2004-2005	Member, Model Systems Review Panel, National Institute on Disability and Rehabilitation Research
2004-2005	President, Division 22 (Rehabilitation Psychology), American Psychological Association
2004-2005	President, American Congress on Rehabilitation Medicine
2005	Member, Committee to Study the Listing of Impairments and Agency Access to Medical Expertise in the Social Security Disability Determination Process, National Academy of Medicine
2005	Member, Medicare Payment Advisory Commission (MedPAC) Panel on Post-Acute Care
2005	Chair, Planning Meeting Board on Military and Veterans Health, Medical Follow-Up Agency, National Academy of Medicine
2005-2013	Secretary/Treasurer, Foundation for Rehabilitation Psychology (Board service continues)
2006-2013	Member, Board of Scientific Counselors, National Center for Injury Prevention and Control, CDC
2009-present	Member, Standing Committee of Medical Experts to Assist Social Security on Disability Issues, National Academy of Medicine
2013-present	Co-Editor-in-Chief, Archives of Physical Medicine and Rehabilitation

Honors

1998	Harold Yuker Award for Research Excellence (outstanding article in *Rehabilitation Psychology*) with D Hawkins for “Substance abuse and medical complications following spinal cord injury,” 43, 219-231
1998	Fellow, American Psychological Association, Division of Rehabilitation Psychology
2000	Roger Barker Distinguished Career Award, Division 22 (Rehabilitation Psychology), APA, “in recognition of outstanding lifetime contributions to the science of rehabilitation psychology”
2003	Essie Morgan Excellence Award, American Association of Spinal Cord Injury Psychologists and Social Workers
2004	Harold Yuker Award for Research Excellence (outstanding article appearing in *Rehabilitation Psychology*) with NA Doninger for “Predicting community integration following TBI with health and cognitive status measures,” 48, 156-166
2005	Fellow, American Congress of Rehabilitation Medicine
2009	Anthony M. Solomon Lecturer in Clinical Neuropsychology, Rusk Institute of Rehabilitation Medicine, New York, NY
2013	John S. Coulter Lecturer, American Congress of Rehabilitation Medicine
2017	Dembo-Wright Award Lecturer, Rehabilitation Psychology Conference

C. Contribution to Science

1. Evaluating the effectiveness and efficiency of rehabilitation services is a major focus of my research. This topic reflects the major financing changes affecting the medical rehabilitation industry over the past several decades. Fee-for-service payment has been replaced by a prospective payment system in most post-acute care settings. Providers who can organize services to achieve maximum benefit at minimum cost should thrive, while others that fail to assess the needs and rehabilitation potential of the people they serve will not. I sought opportunities with the Uniform Data System for Medical Rehabilitation, the largest data management service for rehabilitation hospitals, to describe and predict the functional improvement of children and adults, which resulted in a series of publications.
    a) **Heinemann A**. Measuring effectiveness of psychological services during medical rehabilitation. Rehabilitation Psychology. 1997;42(2):148.
    b) Chen CC, **Heinemann AW**, Granger CV, Linn RT. Functional gains and therapy intensity during subacute rehabilitation: a study of 20 facilities. Arch Phys Med Rehabil. 2002;83(11):1514-1523. PMID: 12422318.
    c) **Heinemann AW**, Roth EJ, Rychlik K, Pe K, King C, Clumpner J. The impact of stroke practice guidelines on knowledge and practice patterns of acute care health professionals. J Eval Clin Pract. 2003;9(2):203-212. PMID: 12787184.

d) Chen CC, **Heinemann AW**, Bode RK, Granger CV, Mallinson T. Impact of pediatric rehabilitation services on children's functional outcomes. The American journal of occupational therapy : official publication of the American Occupational Therapy Association. 2004;58(1):44-53. PMID: 14763635

2. Early in my academic career, I came to appreciate that instruments developed using item response theory methods offer substantial benefits over classical test theory methods. I sought and received funding from the CDC and NIDILRR to develop Rasch model-based, interval-level function measures that have greater precision and sensitivity than ordinal-level instruments. I helped rehabilitation researchers appreciate that they can diagnose misfitting items and test takers, evaluate rating scale properties and item set dimensionality, and create easy-to-administer *key forms* that allow scoring in the clinic without a computer. My collaboration with Ben Wright and Michael Linacre at the University of Chicago and Carl Granger at SUNY Buffalo led to a series of publications that demonstrated the Functional Independence Measure can form measures of motor and cognitive function. Subsequently, I have worked with many colleagues in the U.S. and overseas to evaluate established and develop new instruments.
    a) **Heinemann AW**, Linacre JM, Wright BD, Hamilton BB, Granger C. Relationships between impairment and physical disability as measured by the functional independence measure. *Arch Phys Med Rehabil.* 1993;74(6):566-573. PMID: 8503745.
    b) Granger CV, Hamilton BB, Linacre JM, **Heinemann AW**, Wright BD. Performance profiles of the functional independence measure. *Am J Phys Med Rehabil.* 1993;72(2):84-89. PMID: 8476548.
    c) Linacre JM, **Heinemann AW**, Wright BD, Granger CV, Hamilton BB. The structure and stability of the Functional Independence Measure. *Arch Phys Med Rehabil.* 1994;75(2):127-132. PMID: 8311667.
    d) **Heinemann AW**, Harvey RL, McGuire JR, Ingberman D, Lovell L, Semik P, Roth EJ. Measurement properties of the NIH Stroke Scale during acute rehabilitation. *Stroke.* 1997;28(6):1174-1180. PMID: 9183346.

3. Participation in activities of choice is a long-term goal of rehabilitation service providers and valued by persons living with disabilities. Employment, volunteering, leisure and recreation, and activities with family and friends are common goals. How to characterize participation outcomes in more sophisticated ways than counting the frequency of engagement or time spent in activities has challenged rehabilitation researchers. Myriad measures have been developed for populations with intellectual, psychiatric, sensory, and physical disabilities, but few have used contemporary measurement approaches. Thus, we lack a *lingua franca* to describe the participation benefits of rehabilitation. I worked with Spinal Cord and Traumatic Brain Injury Model Systems collaborators and others to organize an international conference that defined optimal approaches to measuring participation outcomes.
    a) Whiteneck GG, Dijkers MP, **Heinemann AW**, Bogner JA, Bushnik T, Cicerone KD, Corrigan JD, Hart T, Malec JF, Millis SR. Development of the Participation Assessment with Recombined Tools-Objective for Use After Traumatic Brain Injury. *Archives of Physical Medicine and Rehabilitation.* 2011;92(4):542-551. PMID: 21367393
    b) Wong AW, **Heinemann AW**, Wilson CS, Neumann H, Fann JR, Tate DG, Forchheimer M, Richards JS, Bombardier CH. Predictors of participation enfranchisement after spinal cord injury: the mediating role of depression and moderating role of demographic and injury characteristics. *Arch Phys Med Rehabil.* 2014;95(6):1106-1113. PMID: 24561060

4. The lived experience of disablement in community settings, particularly quality of life, is a recurring theme of my work. It is important to look beyond the brief period of inpatient or outpatient rehabilitation services to a life in the community. Two RRTCs explored the precursors and consequences of impairment and functional limitations on the quality of life of adults with physical disabilities. My collaborators and I developed a measure of participation, the Community Participation Indicators, during the first RRTC and a set of environmental factor measures using item response theory methods during the second RRTC. This work built on my early involvement in the PROMIS network, which led to development of quality of life measures for persons with neurologic disorders (NeuroQoL) and then for traumatic brain injury and spinal cord injury.
    a) **Heinemann AW**, Magasi S, Hammel J, Carlozzi NE, Garcia SF, Hahn EA, Lai JS, Tulsky D, Gray DB, Hollingsworth H, Jerousek S. Environmental Factors Item Development for Persons with Stroke, Traumatic Brain Injury and Spinal Cord Injury. Arch Phys Med Rehabil, 96(4) 589-595 DOI: http://dx.doi.org/10.1016/j.apmr.2013.11.024. PMCID: PMC4593403.
    b) **Heinemann AW**, Magasi S, Bode RK, Hammel J, Witeneck GG, Bogner J, Corrigan JD. Measuring enfranchisement: importance of and control over participation by people with disabilities. *Arch Phys Med Rehabil.* 2013;94(11):2157-2165. PMID: 23769764.

c) Tulsky DS, Kisala PA, Lai JS, Carlozzi N, Hammel J, **Heinemann AW**. Developing an Item Bank to Measure Economic Quality of Life for Individuals with Disabilities. *Arch Phys Med Rehabil.* 2014.PMID: 24736400
d) Garcia SF, Hahn EA, Magasi S, Lai JS, Semik P, Hammel J, **Heinemann AW**. Development of Self-Report Measures of Social Attitudes that Act as Environmental Barriers and Facilitators for People with Disabilities. Arch Phys Med Rehabil, 96(4) 596-603 DOI: http://dx.doi.org/10.1016/j.apmr.2014.06.019. PMCID: PMC4297740.

5. Research capacity building has been an important focus of my professional activities since I competed successfully for a rehabilitation-focused, health services research-training grant in 1998. Since then, I have renewed the 5-year Advanced Rehabilitation Research Training award from NIDILRR on three occasions, in synchrony with renewal of a T32 award from AHRQ led by Jane Holl, Director, Center for Healthcare Studies and Director, Center for Education in Health Sciences in Northwestern's Institute for Public Health and Medicine. Because of this success, I was invited by NIDILRR staff to serve as keynote speaker at two national capacity-building conferences. I have served as a keynote speaker on research training topics at the Rehabilitation Medicine Summit sponsored by the Foundation for PM&R in 2005 and a National Center for the Dissemination of Disability Research sponsored Task Force on Systematic Review and Guidelines.
   a) Bode R, **Heinemann AW**, Chen D. Measuring the impairment consequences of spinal cord injury. *American Journal of Physical Medicine & Rehabilitation.* 1999;78(6):582-594. PMID:10574175.
   b) Deutsch A, Granger C, Fiedler R, DeJong G, KaneRL, Ottenbacher KJ, **Heinemann AW**, Naughton JP, Trevisan M. Outcomes and reimbursement of inpatient rehabilitation facilities and subacute rehabilitation programs for medicare beneficiaries with hip fracture. *Medical Care.* 2005;43(9):892-901. PMID: 16116354.
   c) Mallinson TR, Manheim LM, Almagor O, Demark HM, **Heinemann AW**. Trends in the supply of inpatient rehabilitation facilities services: 1996 to 2004. *Arch Phys Med Rehabil.* 2008;89(11):2066-2079. PMID: 18996234
   d) Kozlowski AJ, **Heinemann AW**. Using individual growth curve models to predict recovery and activities of daily living after spinal cord injury: an SCIRehab project study. *Arch Phys Med Rehabil.* 2013;94(4 Suppl):S154-164 e151-154. PMID: 23527771

Complete List of Published Work

https://www.ncbi.nlm.nih.gov/sites/myncbi/allen.heinemann.1/bibliography/47569747/public/?sort=date&direction=descending

D. Research Support

Active Projects

DOD W81XWH-17-1-0157 (Heinemann) 9/1/17-8/31/19
Evaluating the Utilization and Efficiency of Wearable Exoskeletons for SCI Rehabilitation
Goal of this application is to acquire information that will guide patient evaluation strategies, training strategies, and clinical decision plans to enable the safe and effective use of robotic exoskeletons to enhance mobility in Veterans and civilians with SCI.

NIDILRR 90SI5022-01-00 (Chen/Heinemann) 9/30/16-9/29/21
The Midwest Regional Spinal Cord Injury Model System
The goal of this project is to investigate the effect of acute intermittent hypoxia alone and in combination with high-intensity task-specific training on upper extremity function in individual with chronic incomplete cervical SCI.

DOD/CDMRP W81XWH-16-1-0788 (Heinemann) 9/30/16-9/29/19
Enhancing quality of orthotic services with process and outcome information
Goal of this project is to help the Defense Health Program improve understanding of the benefits of orthotic devices, treatments, and rehabilitation strategies.

Craig H. Neilsen Foundation (Heinemann) 5/1/16 – 4/30/19
Implementing SCI-QOL into Clinical Practice to Enhance Patient Engagement
This application adapts and evaluates implementation strategies designed to promote routine use of PROs in SCI rehabilitation.

NIDILRR 90DP0025-01-00 (Boninger) 10/01/12-9/29/18
Collaboration on Mobility Training (COMIT) Role: Co-Investigator
Goal of the project is to evaluate effectiveness of training in wheeled mobility at multiple sites

Craig H. Neilsen Foundation (Kisala) 4/30/16-4/30/19
Clinical Adaption of the SCI-QOL Psychosocial Measures Role: Site PI
Goal of this project is to improve psychosocial outcomes such as emotional well-being and quality of life in individuals with SCI.

NIDILRR H133P130013 (Heinemann) 10/1/13-9/30/18
Advanced Rehabilitation Research Training in Health Services Research
Goal of this project/Specific Aims: The goal of this project is to provide an integrated, interdisciplinary, collaborative training program for early career scholars focusing on rehabilitation-related health services research.

Recently Completed Projects

NIDILRR 90SI5009-02-00 (Chen/Heinemann) 10/01/11 – 09/29/17
Midwest Regional Spinal Cord Injury Care System
The goals of MRSCICS are to advance the outcomes of our previous Model Systems research, continue to study the effectiveness of innovative treatment strategies; and evaluate the benefits of a well-designed, comprehensive, coordinated, interdisciplinary continuum of care that lead to improved outcomes for persons with SCI.

AHRQ 5K12HS023011-01 (Cella) 9/1/14-7/31/17
Northwestern University Patient-Centered Intervention and Engagement Training Role: Mentor
Goal of this project is to provide a clear path to independence beginning with an innovative idea, that is, to identify the global problem of adherence to the attributes that are associated with adherence, apply preference weights tot the relative importance of these attributes using choice modeling, and build patient-centered physical activity recommendations based on an individual's preferred attributes.

CD-12-11-4201 Supplement (Heinemann) 9/01/13 – 07/31/17
Patient Centered Outcomes Research Institute (PCORI)
The goal of this project is evaluate the feasibility of developing quality measures from patient-reported outcome measures.

Dept. of Veteran Affairs VA69D-15-C-0107 (Heinemann) 12/01/2014-11/30/2015
Functional Needs Assessment in Persons with SCI
Goal: Consult on measurement and outcome issues in career development award

NIH R24HD065702 (Ottenbacher) 7/01/2010-5/31/2015
Univ. of Texas Medical Branch (UTMB)
Center for Rehabilitation Research Using Large Datasets Role: Co-I
Goal: Provide mentoring services to scientists seeking to improve knowledge of how to use large datasets

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contr butors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Leora R. Cherney

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Professor, Physical Medicine and Rehabilitation & Communication Sciences and Disorders; Scientific Chair, Think & Speak Lab, Shirley Ryan AbilityLab

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Cape Town, Cape Town, South Africa	B.A.	1978	Logopaedics
Northwestern University, Evanston, IL	M. A.	1980	Speech-Language Pathol
Northwestern University, Evanston, IL	Ph.D.	1990	Speech-Language Pathol

A. Personal Statement

I am well-prepared to serve as Co-PI on this R01 submission. My professional research career of 35+ years has focused on communication problems associated with stroke, with expertise in the area of aphasia. I founded the Aphasia Center at the Rehabilitation Institute of Chicago in 2001, and the past 15+ years have been devoted specifically to developing innovative treatments for aphasia and evaluating their efficacy. I have a continuous record as PI on federal, private, and industry-sponsored research grants, including an NIH R01 and five NIDILRR field-initiated studies. The various topics of my research include: studies assessing the delivery of treatment using novel software with a digital therapist given face-to-face and over the internet; a clinical trial evaluating the addition of a pharmacologic agent, L-dopa, to behavioral language therapy; and studies examining how acquisition can be optimized and forgetting minimized by manipulating various treatment parameters that affect how people with aphasia learn. I led a study examining the effects of epidural cortical stimulation combined with speech-language therapy for aphasia and have held an R21 evaluating on-line tDCS combined with speech therapy in a small group of subjects with aphasia. I have a demonstrated record of successful, productive and cutting-edge research in the area of aphasia treatment that includes both single-subject research studies and randomized clinical trials, and that measures outcomes relative to both impairment and participation levels. I have worked collaboratively with Drs. Heinemann, Kocherginsky, and Baliki, and have published in the area of aphasia with each of these colleagues. I have the research expertise, administrative skills, and clinical knowledge of rehabilitation, aphasia and outcomes to ensure the successful completion of this multi-site longitudinal study.

Cherney, L. R., Babbitt, E. M., Semik, P., & Heinemann, A. W. (2011). Psychometric Properties of the Communication Confidence Rating Scale for Aphasia (CCRSA): Phase 1. Topics in Stroke Rehabilitation, 18, 352-360. doi: 10.1310/tsr1804-352

Cherney, L. R., Kaye, R. C., & van Vuuren, S. (2014). Acquisition and maintenance of scripts in aphasia: a comparison of two cuing conditions. Am J Speech Lang Pathol, 23(2), S343-360. 10.1044/2014_AJSLP-13-0097

Babbitt, E. M., Worrall, L. E., & **Cherney, L. R**. (2016). Intensive Comprehensive Aphasia Programs (ICAP): Who benefits? Topics in Language Disorders. 36, 168-184. 10.1097/TLD.0000000000000089

Lee, J. B., Kocherginsky, M., & **Cherney, L. R.** (2018) Attention in Individuals with Aphasia: Performance on the Conners' Continuous Performance Test-2nd Edition. Neuropsychological Rehabilitation. Published online: 18 Apr 2018. doi.org/10.1080/09602011.2018.1460852

B. Positions and Honors

1981-1986	Staff Speech Language Pathologist, Department of Communicative Disorders, Rehabilitation Institute of Chicago, Chicago, Illinois.
1986- 1996	Clinical Researcher, Communicative Disorders, Rehabilitation Institute of Chicago
1987-1988	Consultant/Clinical Instructor, Physical Medicine and Rehabilitation, Chicago Neurosurgical Center, Chicago, IL
1988-89, 2000-02	Instructor, Department of Communicative Disorders, Northern Illinois University, DeKalb, IL
1990-1996	Assistant Professor, Physical Medicine and Rehabilitation, Northwestern University Medical School, Chicago, IL
1992, 1994-1998	Adjunct, Communication Sciences and Disorders, Northwestern University, Evanston, IL
1996-2002	Clinical Educator, Center for Clinical Excellence, Rehabilitation Institute of Chicago, Chicago, IL
1996-2009	Associate Professor, Physical Medicine and Rehabilitation, Northwestern University Medical School, Chicago, IL
1999-2010	Associate Professor, Communication Sciences & Disorders, Northwestern University, Evanston, Illinois.
2002-2017	Research Scientist/Senior Research Scientist, Rehabilitation Institute of Chicago, Chicago, IL
2009-present	Professor, Physical Medicine and Rehabilitation, Northwestern University Medical School, Chicago, IL
2011-present	Professor, Communication Sciences and Disorders, Northwestern University, Evanston, IL
2017-present	Scientific Chair & Coleman Foundation Chair, Think & Speak, Shirley Ryan AbilityLab, Chicago, IL

Board Certified – Academy of Neurologic Communication Disorders and Sciences
Fellow, American Speech-Language-Hearing Association; Fellow and Honors, Illinois Speech-Language Hearing Association.
Editorial Board, Aphasiology, Archives of Physical Medicine & Rehabilitation, Topics in Stroke Rehabilitation.
Veterans Administration grant review panel: Sensory Systems and Communication, August, 2011, March 2012, August 2012, February 2013.
National Institutes of Health Grant Review Panels: December 2013, March 2014, January & September 2015.
2017 ACRM / National Stroke Association Excellence in Post-Acute Stroke Award. Recognizes outstanding clinical, intellectual, and service contributions in the area of stroke.

C. Contributions to Science

1. The literature on upper limb recovery after focal cortical injury in both animal models and human stroke survivors suggests that high intensity rehabilitation is necessary to induce neuroplasticity. The extent to which these findings translate to the treatment of aphasia is not clear. In 2008 and 2010, my colleagues and I completed systematic reviews of the literature and concluded that intensive treatment was favored over less intensive treatment, but differences in the chronicity of the aphasia (acute versus chronic) and the targeted level of the outcome measure (impairment versus activity/participation) influenced findings. In my own research, we have demonstrated neurophysiological changes on fMRI following treatment and have found a positive correlation between treatment intensity and outcomes, a topic that many researchers continue to investigate with regards to the treatment of aphasia.
    a. **Cherney, L. R.** & Small, S. L. (2006). Task-dependent changes in brain activation following therapy for nonfluent aphasia: Discussion of two individual cases. Journal of the International Neuropsychological Society, 12, 828-842. doi.org/10.1017/S1355617706061017
    b. **Cherney, L. R**., Patterson, J., Raymer, A., Frymark, T., & Schooling, T. (2008). Evidence-Based Systematic Review: Effects of Intensity of Treatment and Constraint-Induced Language Therapy for Individuals with Stroke-Induced Aphasia. Journal of Speech, Language, and Hearing Research, 51, 1282-1299. doi: 10.1044/1092-4388(2008/07-0206)

c. Lee, J. B., Kaye, R. C., **Cherney, L. R.** (2009). Conversational script performance in adults with non-fluent aphasia: Treatment intensity and aphasia severity. Aphasiology, 23(7), 885-897. 10.1080/02687030802669534

d. **Cherney, L. R.** (2012). Aphasia treatment: Intensity, dose parameters, and script training. International Journal of Speech-Language Pathology, 14, 424-31. doi.org/10.3109/17549507.2012.686629

2. Researchers are investigating ways to enhance treatment outcomes in aphasia rehabilitation. Cortical stimulation may be an adjuvant to speech and language treatment to facilitate neuroplasticity. There are several methods of delivering cortical brain stimulation to modulate cortical excitability. I conducted the only controlled study evaluating targeted epidural cortical delivered concurrently with intensive speech–language therapy for treatment of chronic non-fluent aphasia. Six weeks of epidural cortical stimulation to the ipsilesional premotor cortex in combination with speech and language treatment was feasible, safe, and promoted increased improvements as compared to the control group that received speech and language treatment without cortical stimulation. This study has informed other studies that investigate less invasive methods of cortical stimulation.

a. **Cherney, L. R**., Erickson, R. K., & Small, S. L. (2010). Epidural Cortical Stimulation as Adjunctive Treatment for Non-Fluent Aphasia: Preliminary Findings. Journal of Neurology, Neurosurgery, and Psychiatry, 81(9), 1014-1021. 10.1136/jnnp.2009.184036

b. **Cherney, L. R.,** Harvey, L. R., Babbitt, E. M., Hurwitz, R., Kaye, R. C., Lee, J. B., & Small, S. L. (2012). Epidural cortical stimulation and aphasia therapy. Aphasiology, 26(9), 1192-1217. 10.1080/02687038.2011.603719

c. **Cherney, L. R.** (2016). Epidural Cortical Stimulation as Adjunctive Treatment for Nonfluent Aphasia: Phase 1 Clinical Trial Follow-up Findings. Neurorehabil Neural Repair, 30(2), 131-42. doi.org/10.1177/1545968315622574

d. **Cherney, L. R.,** Babbitt, E. M., Hurwitz, R., Rogers, L. M., Wang, X., Harvey, R. L., Parrish, T., & Stinear, J. (2013). Transcranial Direct Current Stimulation (tDCS) and Aphasia: The Case of Mr. C. Topics in Stroke Rehabilitation, 20(1).5-21. doi.org/10.1310/tsr2001-5

3. Since it appears that better outcomes result from more intensive treatment, I have been investigating how we can leverage technology to provide more intensive and cost-effective treatment. I have led an initiative to develop and computerize several treatment approaches and we are investigating their efficacy. Results to date have been positive. Participants are able to practice intensively with improved outcomes. The scientific impact has been two-fold – our studies have stimulated interest in computer-based treatment in general, and more specifically, there has been increased attention to the particular treatments that have been developed, with further investigation of these treatments by others.

a. **Cherney, L. R.,** Halper, A. S., Holland, A. L. & Cole, R. (2008). Computerized Script Training for Aphasia: Preliminary Results. American Journal of Speech-Language Pathology, 17, 19-34**.** 10.1044/1058-0360(2008/003)

b. Mannheim, L., Halper, A. S. & **Cherney, L. R.** (2009). Patient-Reported Changes in Communication after Computer-Based Script Training for Aphasia. Archives of Physical Medicine and Rehabilitation, 90(4), 623-627. 10.1016/j.apmr.2008.10.022

c. **Cherney, L. R.** (2010). Oral Reading for Language in Aphasia (ORLA): Evaluating the Efficacy of Computer-Delivered Therapy in Chronic Nonfluent Aphasia. Topics in Stroke Rehabilitation, 17(6), 423-431. 10.1310/tsr1706-423

d. Kaye, R. C. & **Cherney, L. R.** (2016). Script templates: A practical approach to script training in aphasia. Topics in Language Disorders, 2016; 36:136-153. doi: 10.1097/TLD.0000000000000086

4. More recently, there has been an emphasis on patient-reported outcomes. I led the development of a patient-reported outcome scale that addresses not just communication in persons with aphasia, but

communication confidence. This construct, associated with self-efficacy, had not previously been discussed in the aphasia literature. The assessment tool, the Communication Confidence Rating Scale for Aphasia (CCRSA), was developed and validated using Rasch Analysis methods. It is currently being used by researchers in the United States, Canada, England, and Australia.

a. Babbitt, E.M. & **Cherney, L. R.** (2010). Communication Confidence in Persons with Aphasia. Topics in Stroke Rehabilitation, 17(3), 197-206. 10.1310/tsr1703-214
b. **Cherney, L. R.,** Babbitt, E. M., Semik, P., & Heinemann, A. W. (2011). Psychometric Properties of the Communication Confidence Rating Scale for Aphasia (CCRSA): Phase 1. Topics in Stroke Rehabilitation, 18, 352-360. doi: 10.1310/tsr1804-352
c. Babbitt, E.M., Heinemann, A. W., Semik, P., & **Cherney, L. R.** (2011). Psychometric Properties of the Communication Confidence Rating Scale for Aphasia (CCRSA): Phase 2. Aphasiology, 25, 727-735. doi.org/10.1080/02687038.2010.537347

5. The intensive comprehensive aphasia program (ICAP) is a service-delivery model that, based on the notion of neuroplasticity, provides intensive treatment to persons with aphasia. At the same time, it addresses all domains of the ICF including the impairment and the activity/participation domains. There has been relatively little research regarding the efficacy, effectiveness and cost-effectiveness of the ICAP, although more and more clinical programs, nationally and internationally, are offering such services. Since 2011, I have spear-headed an initiative that introduced its acronym, defined its characteristics, and identified research gaps and recommendations for future investigations. This has resulted in several ongoing studies within the scientific community, including an RCT on which I am currently the PI.
   a. Rose, M. L., **Cherney, L. R**., & Worrall, L. E. (2013). Intensive Comprehensive Aphasia Programs: An international survey of practice. Topics in Stroke Rehabilitation, 20, 379-387. 10.1310/tsr2005-379
   b. Babbitt, E. M., Worrall, L. E., & **Cherney, L. R.** (2013). Clinician perspectives of an Intensive Comprehensive Aphasia Program. Topics in Stroke Rehabilitation, 20, 398-408. 10.1310/tsr2005-398
   c. Hula, W. D., **Cherney, L. R.**, & Worrall, L. E. (2013). Setting a research agenda to inform Intensive Comprehensive Aphasia Programs. Topics in Stroke Rehabilitation, 20, 409-420. 10.1310/tsr2005-409
   d. Babbitt, E. M., Worrall, L., & **Cherney, L. R.** (2015). Structure, processes, and retrospective outcomes from an intensive comprehensive aphasia program. American Journal of Speech Language Pathology, 24(4), S854-63. 10.1044/2015_AJSLP-14-0164

My bibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/leora.cherney.1/bibliography/43924728/public/?sort=date&direction=ascending and
http://scholar.google.com/citations?user=-UgIYgkAAAAJ&hl=en

D. Research Support

ACTIVE

The Carl & Marilynn Thoma Foundation (Cherney) 3/01/2018 – 2/28/2023
Brain Network Properties and Intensive Aphasia Therapy
This project uses resting state fMRI in persons with aphasia before and after they receive intensive aphasia treatment to examine specific brain network properties and determine their role in predicting responsiveness to treatment.
Role: Principal Investigator

90IFRE0007-01-00 (Cherney) 10/01/2017 – 9/30/2020
NIDILRR Field Initiated Program
Improving electronic written communication in persons with aphasia: A clinical trial

This project evaluates the extent to which a novel treatment (T-WRITE) improves hand-written language versus text messaging in persons with aphasia, and assesses whether there are subsequent positive effects on the participant's social connectedness and ultimately health-related quality of life (HRQOL).
Role: Principal Investigator

H133B140012 (Roth) 10/01/2014 – 9/30/2019
NIDILRR Rehabilitation Engineering Research Center
Project 3: The Intensive Comprehensive Aphasia Program (ICAP): A Randomized Clinical Trial
This study is a randomized clinical trial that compares the efficacy and cost-effectiveness of an ICAP that provides 60 hours of intensive treatment over three weeks (i.e. 4 hours a day, 5 days a week for 3 weeks) to rehabilitation that provides the same amount and type of comprehensive treatment but is distributed over 15 weeks (i.e. 2 hours, twice a week for 15 weeks).
Role: Principal Investigator on Project 3

H133E130019 (Rymer) 10/01/2013 – 9/30/2018
NIDILRR Rehabilitation Engineering Research Center
Project 2: Time Distribution of Computer-Based Script Training in Aphasia
This project conducts a series of intervention studies to examine the rate and extent to which persons with aphasia learn and subsequently forget, following one or more treatment sessions. Mathematical modeling will develop algorithms to predict best outcomes based on treatment schedules. Then we explore how clinicians utilize these algorithms together with patient performance data from each session to make clinical decisions about the timing of subsequent sessions.
Role: Principal Investigator on Project 2

H133P120013 (Cherney) 10/01/2012 - 9/30/2018
NIDILRR Advanced Rehabilitation Research Training Program (ARRT)
Interventions for Neurologic Communication Disorders
This training grant provides two years of intensive training to post doctoral fellows who are committed to a career in rehabilitation research. It provides training in the development of skills necessary to conduct high quality independent interdisciplinary funded research in the rehabilitation of clinical populations with communication disorders that accompany neurological conditions including stroke, traumatic brain injury, and Parkinson's disease.
Role: Principal Investigator/Project Director

<u>COMPLETED (in last 2 years)</u>

1R01DC011754 (Cherney) 07/08/2011 – 12/30/2017
NIH/NIDCD
Aphasia Rehabilitation: Modulating Cues, Feedback & Practice
We are conducting a series of intervention studies to examine how different treatment variables (cues, feedback, task complexity) and practice conditions (blocked/random, massed/distributed) affect short-term acquisition and long-term maintenance and generalization of a skill in the rehabilitation of chronic aphasia.
Role: Principal Investigator

H133G120123 (Cherney) 10/01/2012 – 9/30/2016
NIDILRR Field Initiated Program
Enhancing Written Communication in Persons with Aphasia: A Clinical Trial
This randomized controlled trial for persons with chronic aphasia evaluates the efficacy of an intensive computer-based treatment program that targets sentence-level oral and written language skills.
Role: Principal Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Domenighetti, Andrea Alberto

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Research Scientist and Assistant Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Geneva - Switzerland	BSc	10/1997	Biology
University of Geneva - Switzerland	DipSc	03/1998	Vascular biology
University of Melbourne - Australia	PhD	12/2006	Muscle cell biology & physiology
University of California, San Diego - USA	Post-doc	12/2010	Muscle cell biology & physiology

A. Personal Statement

As a principal investigator (PI) at the Shirley Ryan AbilityLab (SRAlab), I aim to identify new mechanisms relating to muscle tissue and muscle stem cell dysfunction, as well as genetic and epigenetic modifications affecting muscle and nerve plasticity in patients with spinal cord and brain injury (cerebral palsy and stroke). Before joining the SRAlab in 2015, I spent 15+ years training and working in leading academic Institutes around the world, including the University of California in San Diego (UCSD), the University of Lausanne (Switzerland) and the University of Melbourne (Australia). During these years, my scientific work and interests focused on molecular and cellular mechanisms associated with cardiac muscle diseases and skeletal muscle dysfunction, creating or using animal models, isolated cells, electrophysiology, video imaging, functional genomic and molecular biology. Since 2014, my research interests have shifted towards more translational research, relevant to brain and spinal cord injury, as well as neuromuscular disorders. My current group of research is fully integrated into the Biologics Lab at the SRAlab and in the PM&R Department at Northwestern University. I strongly believe that the combination of my long-standing experience working with molecular, genomic, biochemical assays, as well as patient biopsies would make my group highly suitable to support the genetic analyses proposed for this project. We have already optimized the SNP assays proposed in this application and my lab is currently using these same assays in separate clinical studies investigating therapy outcomes in patients with spinal cord injury and stroke. The following three publications reflect some of the depth and breadth that I have accumulated over the years as an experimental biologist and physiologist, but also as a research scientist highly concerned with clinical outcomes and therapeutic approaches for patients.

i. **Domenighetti AA**, Chu PH, Wu T, Sheikh F, Gokhin DS, Guo LT, Cui Z, Peter AK, Christodoulou DC, Parfenov MG, Gorham JM, Li DY, Banerjee I, Lai X, Witzmann FA, Seidman CE, Seidman JG, Gomes AV, Shelton GD, Lieber RL, Chen J. Loss of FHL1 induces an age-dependent skeletal muscle myopathy associated with myofibrillar and intermyofibrillar disorganization in mice. Hum Mol Genet. 2014;23(1):209-25. PMID: 23975679; PMCID: 3916749.

ii. Feingold B, Mahle WT, Auerbach S, Clemens P, **Domenighetti AA**, Jefferies JL, Judge DP, Lal AK, Markham LW, Parks WJ, Tsuda T, Wang PJ, Yoo SJ; American Heart Association Pediatric Heart Failure Committee of the Council on Cardiovascular Disease in the Young; Council on Clinical Cardiology; Council on Cardiovascular Radiology and Intervention; Council on Functional Genomics and Translational Biology; and Stroke Council. Management of Cardiac Involvement Associated With Neuromuscular Diseases: A

Scientific Statement From the American Heart Association. Circulation. 2017 Aug 24 [Epub ahead of print] PMID: 28838934.

iii. **Domenighetti AA**, Mathewson MA, Pichika R, Sibley LA, Zhao L, Chambers HG, Lieber RL. Loss of myogenic potential and fusion capacity of muscle stem cells isolated from contractured muscle in children with cerebral palsy. Am J Physiol Cell Physiol. 2018. doi: 10.1152/ajpcell.00351.2017. PubMed PMID: 29694232.

B. Positions and Honors

Positions and Employment

1998-1999: Research Assistant – Division of Hypertension, Lausanne University Hospital, Switzerland.
1999-2004: PhD fellow - Department of Physiology, The University of Melbourne, Australia.
2004-2006: Research Associate and PhD fellow, Department of Pharmacology & Toxicology, University of Lausanne, Switzerland.
2007-2010: Postdoctoral fellow - Department of Medicine, Cardiology, University of California, San Diego.
2011-2013: Assistant Project - Department of Medicine, Cardiology, University of California, San Diego.
2014-2015: Assistant Project - Department of Orthopaedic Surgery, University of California, San Diego.
2015-pres: Research Scientist– Rehabilitation Institute of Chicago/Shirley Ryan AbilityLab.
2015-pres: Research Assistant Professor – Department of Physical Medicine & Rehabilitation, Northwestern University.

Other Experience and Professional Memberships

1995-1997: President elected of the Biology Student Association – University of Geneva.
1995-1998: Member elected of the Geneva University Council. Student representative.
1997-1998: Member elected of the Council of the Faculty of Sciences at Geneva University.
2000-2005: Member of the Australian Physiological & Pharmacological Society (APPS).
2001-2002: Member elected of the board of the APPS. Postgraduate representative.
2002-2005: Member of the Australasian Section of the International Society of Heart Research (ISHR).
2003-2010: Member of the Swiss Cardiovascular Research and Training Network.
2010-2015: Member of the American Section of the ISHR.
2007-pres.: Professional member of the American Heart Association (AHA).
2009-pres.: Member of the American Society for Cell Biology (ASCB).
2015-pres.: Member of the Orthopaedic Research Society (ORS).
2016-pres.: Member of the Society for Muscle Biology.

Honors:

1998-1999: Research Fellowship from the Roche Research Foundation.
2000-2004: International Postgraduate Research Scholarship (IPRS) and Melbourne International Research Scholarship (MIRS) from the University of Melbourne.
2000-2001: Young Researcher/Doctoral Fellowship from the Swiss National Science Foundation.
2001: Young Investigator Travel Award from the IUPS (International Union of Physiological Sciences).
2002: W.G. Nayler Prize (Award for the best scientific presentation at the ISHR - Australia).
2004: Novartis Prize for the best scientific presentation at the 10th Cardiovascular Biology and Clinical Implications Meeting, Thun - Switzerland.
2007: Pfizer Excellence Award in Cardiovascular Research – Switzerland.
2007-2009: Advanced Postdoctoral Fellowship from the Swiss National Science Foundation.
2011: Elected Fellow of the American Heart Association (FAHA).
2013: Life Technologies Prize for best poster presentation, 1st Alternative Muscle Club Conference, San Diego, CA
2015: Award for best poster presentation, 3rd Alternative Muscle Club Conference, Tucson, AZ.

C. Contribution to Science

1. I started my scientific career at the University of Geneva in Switzerland where I obtained a Diploma degree in Biology examining vasodilatory intercellular calcium waves, propagating through gap junctions in coronary endothelial cell cultures *in vitro*. After my degree, I moved to the Division of Hypertension at the University of Lausanne (Switzerland). As a Research Assistant, I collaborated on investigations looking at the role of neuroendocrine activation in the development of myocardial dysfunction, using tissue-isolated mouse neonatal cardiomyocytes *in vitro*.

   i. **Domenighetti AA**, Beny JL, Chabaud F, Frieden M. An intercellular regenerative calcium wave in porcine coronary artery endothelial cells in primary culture. J Physiol. 1998;513 (Pt 1):103-16. PMID: 9782162; PMCID: PMC2231269.
   ii. Pellieux C, Sauthier T, **Domenighetti A**, Marsh DJ, Palmiter RD, Brunner HR, Pedrazzini T. Neuropeptide Y (NPY) potentiates phenylephrine-induced mitogen-activated protein kinase activation in primary cardiomyocytes via NPY Y5 receptors. Proc Natl Acad Sci U S A. 2000;97(4):1595-600. PMID: 10660688; PMCID: PMC26480.

2. After obtaining scholarships and fellowships from both industry (Roche) and academic entities (the University of Melbourne and the Swiss National Science Foundation), I was able to join the Department of Physiology at the University of Melbourne in Australia, from which I obtained my PhD degree. During my PhD training, I developed and used various techniques of video imaging, single cell contractility, electrophysiology and cDNA microarrays to investigate genome-wide gene expression profiles and mechanisms of excitation-contraction coupling regulating cardiac myocytes function during agonist- and metabolism-induced heart failure in mice. After my PhD training, I worked as a Research Associate in the Department of Pharmacology & Toxicology at the University of Lausanne. During this time, I successfully exchanged and implemented my skills in cell biology and functional genomics, using microarrays to study new candidate genes responsible for the development of angiotensin-induced heart failure and developing EKG measurements on mouse models of cardiac hypertrophy and heart failure.

   i. **Domenighetti AA**, Wang Q, Egger M, Richards SM, Pedrazzini T, Delbridge LM. Angiotensin II-mediated phenotypic cardiomyocyte remodeling leads to age-dependent cardiac dysfunction and failure. Hypertension. 2005;46(2):426-32. PMID: 15998712.
   ii. Gavillet B, Rougier JS, **Domenighetti AA**, Behar R, Boixel C, Ruchat P, Lehr HA, Pedrazzini T, Abriel H. Cardiac sodium channel Nav1.5 is regulated by a multiprotein complex composed of syntrophins and dystrophin. Circ Res. 2006;99(4):407-14. PMID: 16857961.
   iii. Croquelois A, **Domenighetti AA***, Nemir M, Lepore M, Rosenblatt-Velin N, Radtke F, Pedrazzini T. Control of the adaptive response of the heart to stress via the Notch1 receptor pathway. J Exp Med. 2008;205(13):3173-85. PMID: 19064701; PMCID: PMC2605223 **(* co-first authorship)**.
   iv. Wang Q, **Domenighetti AA***, Schafer SC, Weber J, Simon A, Maillard MP, Pedrazzini T, Chen J, Lehr HA, Burnier M. Impact of salt on cardiac differential gene expression and coronary lesion in normotensive mineralocorticoid-treated mice. Am J Physiol Regul Integr Comp Physiol. 2012;302(9):R1025-33. PMID: 22403797 **(* co-first authorship)**.

3. After receiving an advanced post-doctoral fellowship from the Swiss National Science Foundation, I joined the University of California, San Diego (UCSD). I focused my research on cardiac complications and skeletal muscle dysfunction associated with absence of the LIM-only domain protein FHL1 in FHL1-null mice. After successfully writing and obtaining a NIH-R21 grant for the laboratory (to produce new FHL1-mutant mouse models mimicking disease-causing point mutations in patients), I was promoted to assistant Project Scientist at the UCSD. During my tenure in Cardiology, I also developed and created genetically-modified mouse models to study the effects of clinically-relevant FHL1 mutations on cardiac function and development of muscle impairment.

   i. Sheikh F, Raskin A, Chu PH, Lange S, **Domenighetti AA**, Zheng M, Liang X, Zhang T, Yajima T, Gu Y, Dalton ND, Mahata SK, Dorn GW, 2nd, Brown JH, Peterson KL, Omens JH, McCulloch AD, Chen J. An FHL1-containing complex within the cardiomyocyte sarcomere mediates hypertrophic biomechanical stress responses in mice. J Clin Invest. 2008;118(12):3870-80. PMID: 19033658; PMCID: PMC2575833.

ii. Bertrand AT, Bonnemann CG, Bonne G, **FHL1 myopathy consortium**. 199th ENMC international workshop: FHL1 related myopathies, June 7-9, 2013, Naarden, The Netherlands. Neuromuscul Disord. 2014;24(5):453-62. PMID: 24613424.
iii. Christodoulou DC, Wakimoto H, Onoue K, Eminaga S, Gorham JM, DePalma SR, Herman DS, Teekakirikul P, Conner DA, McKean DM, **Domenighetti AA**, Aboukhalil A, Chang S, Srivastava G, McDonough B, De Jager PL, Chen J, Bulyk ML, Muehlschlegel JD, Seidman CE, Seidman JG. 5'RNA-Seq identifies Fhl1 as a genetic modifier in cardiomyopathy. J Clin Invest. 2014;124(3):1364-70. PMID: 24509080; PMCID: PMC3934171.
iv. **Domenighetti AA**, Chu PH, Wu T, Sheikh F, Gokhin DS, Guo LT, Cui Z, Peter AK, Christodoulou DC, Parfenov MG, Gorham JM, Li DY, Banerjee I, Lai X, Witzmann FA, Seidman CE, Seidman JG, Gomes AV, Shelton GD, Lieber RL, Chen J. Loss of FHL1 induces an age-dependent skeletal muscle myopathy associated with myofibrillar and intermyofibrillar disorganization in mice. Hum Mol Genet. 2014;23(1):209-25. PMID: 23975679; PMCID: PMC3916749.

4. Since 2014, my research interests have shifted towards <u>preclinical and translational research relevant to striated (cardiac and skeletal) muscles function and regeneration in patients with brain injury, spinal cord injury and neuromuscular disorders</u>. In particular, my laboratory has recently published a manuscript entitled "Loss of myogenic potential and fusion capacity of satellite cells isolated from contractured muscle in children with cerebral palsy" (Am J Physiol). Our study show that muscle contractures in children with cerebral palsy are associated with premature loss of muscle stem cells myogenic potential *in vitro*. Application of specific class of cytidine analogs may revert this phenotype.

i. Blondelle J, Shapiro P, **Domenighetti AA**, Lange S. Cullin E3 Ligase Activity Is Required for Myoblast Differentiation. J Mol Biol. 2017; 429(7):1045-1066. PMID: 28238764; PMCID: PMC5395100.
ii. Feingold B, Mahle WT, Auerbach S, Clemens P, **Domenighetti AA**, Jefferies JL, Judge DP, Lal AK, Markham LW, Parks WJ, Tsuda T, Wang PJ, Yoo SJ; American Heart Association Pediatric Heart Failure Committee of the Council on Cardiovascular Disease in the Young; Council on Clinical Cardiology; Council on Cardiovascular Radiology and Intervention; Council on Functional Genomics and Translational Biology; and Stroke Council. Management of Cardiac Involvement Associated With Neuromuscular Diseases: A Scientific Statement From the American Heart Association. Circulation. 2017 Aug 24 [Epub ahead of print] PMID: 28838934.
iii. **Domenighetti, AA**, Lieber RL. U.S. Provisional Patent App. No. 62/572,609, Methods for Treating Contractured Muscle and Related Cultured Cells.
iv. **Domenighetti AA**, Mathewson MA, Pichika R, Sibley LA, Zhao L, Chambers HG, Lieber RL. Loss of myogenic potential and fusion capacity of muscle stem cells isolated from contractured muscle in children with cerebral palsy. Am J Physiol Cell Physiol. 2018. doi: 10.1152/ajpcell.00351.2017. PubMed PMID: 29694232

Complete List of Published Work:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1ZivfqtckH7/bibliograpahy/40574815/public/?sort=date&direction=ascending

D. Research Support

Ongoing Research Support:

2015-present: startup and lab development fund from the Shirley Ryan AbilityLab.

Completed Research Support:

R24 HD050837 Domenighetti 07/01/2014-06/30/2015
Title: Discovering new epigenetic pathways that regulate skeletal muscle homeostasis
Goal: Startup fund to create a Pax7-specific satellite cell and Tamoxifen-inducible knockout mouse line for EHBP1L1 (Pax7-CreER+/- EHBP1L1LoxP/LoxP) and to define the biological role of EHBP1L1 in isolated satellite cells *in vitro* and adult skeletal muscle *in vivo*.

R21 AR061024 Chen (PI) 07/01/2011-06/30/2013
Title: The role of FHL1 in Emery-Dreifuss and Reducing Body myopathies.
Goal: The goal of this proposal is to understand the role that FHL1 plays in skeletal muscle growth and homeostasis and to understand why different mutations in FHL1 result in different myopathies. Creation of two mutant mouse models recapitulating human FHL1 mutations is proposed.
Role: Assistant Project Scientist

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. DO NOT EXCEED FIVE PAGES.

NAME: Marwan Nabil Baliki

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Research Scientist, Rehabilitation Institute of Chicago

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
American University of Beirut, Lebanon	B.S.	1998	Biology
American University of Beirut, Lebanon	M.S	2001	Neuroscience
Northwestern University, Chicago	Ph.D.	2009	Neuroscience
Northwestern University, Chicago	Post-doctoral fellow	2013	Neuroscience

A. Personal Statement

My research seeks to define the brain neural mechanisms underlying the processing of normal and pathological sensory and cognitive processes in humans. My research encompasses both novel methodological and theoretical constructs that enable us to formulate physiological and behavioral models that allows us to investigate the impact of medical interventions in clinical setting such as identifying brain based biomarkers for onset of symptoms following injury or brain reorganization in response to specific treatments. The majority of my past research focused on the study of chronic pain. Only by providing key neural information about pain, can we explicate the brain process and behavioral changes associated with chronic pain. Pain has been classically studied from the viewpoint of peripheral afferent inputs, spinal cord coding, and brainstem descending modulation. My recent studies utilized state of the art neuroimaging techniques and modelling such as using graph theory to analyze resting state changes in clinical conditions compared to controls. I am looking forward to utilizing my extensive expertise in brain imaging analysis to investigate functional and anatomical reorganization in patients suffering from aphasia. This will allow us to unravel the brain physiological and anatomical properties associated with aphasia, and thus for the first time identify biomarkers that can be used as targets for efficacious therapy and aid in the rehabilitation efforts of people with aphasia. I have been working closely with Dr. Cherney (the co-principle investigator of this proposal) for the past year on several projects that focus on identifying brain networks underlying language expression and comprehension in patients with aphasia. We have already studied more than 40 patients and have a manuscript entitled “Brain network topology influences response to intensive comprehensive aphasia treatment” accepted for publication. The Shirley Ryan Abilitylab provides all necessary tools for the success of this collaboration and project.

B. Position and Honors

Positions and Employment

2000 - 2001 Teaching assistant, Depart of Morphology, American University of Beirut
2001 - 2003 Research Assistant, Department of Physiology, Northwestern University
2012 - 2015 Research Associate, Department of Physiology, Northwestern University
2015 - Research scientist, Shirley Ryan AbilityLab (formerly Rehab. Inst. Of Chicago)
2015 - Assistant Professor, Physical Medicine and Rehabilitation, Northwestern university

Other Experiences and Professional Memberships

2001 -	Member, Society for Neuroscience
2003 -	Member, Human Brain Mapping Member,
2003 -	International Association for the Study of Pain
2005 -	Member, American Pain Society
2016 -	Associate Editor of Pain

C. Contributions to Science

1-Characterization of the brain's network properties

The utility of neuroimaging of health and disease requires an understanding of how the brain dynamically processes complex information flow on local (region to region) and global (module to module) scales. Using graph theory to estimate how information is dynamically shared between and across brain regions, we revealed for the first time that brain activity can be understood as a synchronous network with small world properties. With 964 citations since 2005, this paper has made a seminal contribution across multiple disciplines based on its application of graph theory to brain dynamic properties.

a. Eguíluz VM, Chialvo DR, Cecchi GA, **Baliki MN**, Apkarian AV. Scale-free brain functional networks. Phys Rev Lett. 2005 Jan 14;94(1):018102. PubMed PMID: 15698136.

b. Cecchi GA, Rao AR, Centeno MV, **Baliki MN**, Apkarian AV, Chialvo DR. Identifying directed links in large scale functional networks: application to brain fMRI. BMC Cell Biol. 2007 Jul 10;8 Suppl 1:S5. PubMed PMID: 17634095; PubMed Central PMCID: PMC1924510.

c. **Baliki MN**, Mansour AR, Baria AT, Apkarian AV. Functional reorganization of the default mode network across chronic pain conditions. PLoS One. 2014;9(9):e106133. PubMed PMID: 25180885; PubMed Central PMCID: PMC4152156.

d. Mansour A, Baria AT, Tetreault P, Vachon-Presseau E, Chang PC, Huang L, Apkarian AV, **Baliki MN**. Global disruption of degree rank order: a hallmark of chronic pain.. Sci Rep. 2016 Oct 11;6:34853. PMID: 27725689

2 - Understanding the impact of chronic pain on brain anatomical and functional properties

Advances in imaging technology have enabled non-invasive probing of human brain properties in clinical chronic pain conditions, and our understanding of the brain mechanisms underlying the development and processing of chronic pain is undergoing rapid changes. My work greatly contributed to our current understanding of the brain functional and anatomical reorganization with chronic pain, including the 1) distinguishing brain activity for different clinical pain conditions from each other and acute pain, 2) identifying the impact of brain on default brain functions and resting state dynamics and 3) localizing the association of chronic pain with abnormal structural changes. The impact of my work has resulted in an h index of 35 and at least 6000 citations. I will use my extensive expertise in brain imaging analysis to examine brain functional and anatomical reorganization in patients with aphasia.

a. Chronic pain and the emotional brain: specific brain activity associated with spontaneous fluctuations of intensity of chronic back pain. **Baliki MN**, Chialvo DR, Geha PY, Levy RM, Harden RN, Parrish TB, Apkarian AV. J Neurosci. 2006 Nov 22;26(47):12165-73. PMID: 1712204; PMCID: PMC4177069

b. Beyond feeling: chronic pain hurts the brain, disrupting the default-mode network dynamics. **Baliki MN**, Geha PY, Apkarian AV, Chialvo DR. J Neurosci. 2008 Feb 6;28(6):1398-403. PMID: 18256259

c. The cortical rhythms of chronic back pain. **Baliki MN**, Baria AT, Apkarian AV. J Neurosci. 2011 Sep 28;31(39):13981-90. PMID: 21957259; PMCID: PMC3214084

d. Functional reorganization of the default mode network across chronic pain conditions. **Baliki MN**, Mansour AR, Baria AT, Apkarian AV. PLoS One. 2014 Sep 2;9(9):e106133. doi: 10.1371/journal.pone.0106133. eCollection 2014 . [PubMed - in process], PMID:25180885; PMCID: PMC4152156.

e. Brain morphological signatures for chronic pain. **Baliki MN**, Schnitzer TJ, Bauer WR, Apkarian AV. PLoS One. 2011;6(10):e26010. PMID: 22022493; PMCID: PMC3192794

3 - Identifying a neurobiological model for vulnerability to chronic pain

There are many examples in the clinical literature demonstrating that only a proportion of patients with a particular disease or injury go on to develop chronic pain. I lead the first neuroimaging longitudinal study that enabled us to identify early brain biomarkers that predicted the development of chronic pain with 80% accuracy following an acute back injury. We showed that the functional and anatomical properties within the cortico-limbic system, especially functional and anatomical connectivity between the reward circuitry and frontal brain regions plays an integral part in the transition of acute to chronic pain. These results – and for the first time – alluded that the brain plays an integral part in the development of chronic pain, and provided a neurobiological model that might contribute to the advancement of evidence-based interventions that will greatly enhance strategies for pain management

a. Nociception, Pain, Negative Moods, and Behavior Selection. **Baliki MN**, Apkarian AV.Neuron. 2015 Aug 5;87(3):474-91. doi: 10.1016/j.neuron.2015.06.005. Review. PMID: 26247858; PMCID: PMC4529956

b. Corticostriatal functional connectivity predicts transition to chronic back pain. **Baliki MN**, Petre B, Torbey S, Herrmann KM, Huang L, Schnitzer TJ, Fields HL, Apkarian AV. Nat Neurosci. 2012 Jul 1;15(8):1117-9 PMID: 22751038; PMCID: PMC3411898

c. Resting-state functional reorganization of the rat limbic system following neuropathic injury. **Baliki MN**, Chang PC, Baria AT, Centeno MV, Apkarian AV. Sci Rep. 2014 Sep 2;4:6186. PMID:25178478; PMCID: PMC4151103

Complete List of Published Work

http://www.ncbi.nlm.nih.gov/pubmed/?term=baliki+M

D. Research Support

Active research

Sedgwick Pain Study (Baliki) 1/1/2018 – 12/31/2019
Sedgwick Claims Management Services
Identifying behavioral and brain biomarkers underlying successful pain management and functional rehabilitation in injured workers. Role: Principle Investigator

P50 (Apkarian) 7/1/2018 – 6/30/2023
National Institute of Health
Center for Chronic Pain and Drug Abuse
Role: Co-Investigator

The Carl & Marilynn Thoma Foundation (Cherney) 3/01/2018 – 2/28/2023
Brain Network Properties and Intensive Aphasia Therapy
This project uses resting state fMRI in persons with aphasia before and after they receive intensive aphasia treatment to examine specific brain network properties and determine their role in predicting responsiveness to treatment.
Role: Co-Investigator

Completed research

Fidelity (Baliki) Sep 01, 2009 – Aug 31, 2010
Functional and anatomical changes in different types of chronic pain
Role: Principle Investigator

Nielsen Foundation (Baliki) Sep 01,2016 – Aug 31, 2017
Brain functional and anatomical reorganization in the management of chronic pain
Role: Principle Investigator

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **Elliot J. Roth, MD**

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: **Professor and Chairman, Physical Medicine and Rehabilitation**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Washington University, St. Louis, MO	AB	1978	Chem./Human Serv. Ed
Northwestern Univ. Medical School, Chicago, IL	MD	1982	Medicine
Cook County Hospital, Chicago, IL	Intern	1983	Internal Medicine
Northwestern University Feinberg School of Medicine, Chicago, IL	Resident	1985	Physical Medicine & Rehabilitation
Rehabilitation Institute of Chicago, Chicago, IL	Fellow	1986	Stroke Rehabilitation

A. Personal Statement

Elliot Roth, MD brings more than 25 years of experience in rehabilitation patient care, research, teaching, and program leadership for patients with stroke, traumatic brain injury and other neurological conditions. His research and academic interests are in the areas of novel methods to enhance recovery, improve functional outcomes, and prevent associated medical conditions for people with disabling conditions. He currently is Project Director of a Rehabilitation Research and Training Center on health and function for people with physical disabilities and he recently completed a Rehabilitation Research and Training Center grant on stroke rehabilitation, which he led for 20 years. He is also PI on several other research projects focused primarily on neurorehabilitation. Dr. Roth is the Chairman of the Department of Physical Medicine & Rehabilitation at Northwestern University's Feinberg School of Medicine. In addition to his research and administrative responsibilities, he has an active medical practice, specializing in the care and treatment of patients with a variety of physically disabling conditions, focusing predominantly on the rehabilitation management of patients with stroke. In this study, Dr. Roth will assist with determining subject eligibility as needed across all sites, reviewing clinical MRI scans, and providing input on other medically-related information including medications and the presence of co-morbidities.

B. Positions and Honors

Positions and Employment:

1986-1991 **Assistant Professor,** Physical Medicine and Rehabilitation (PM&R), Northwestern University Feinberg School of Medicine (NUFSM), Chicago, IL
1986- **Attending Physician**, Rehabilitation Institute of Chicago (RIC), Chicago, IL
1986- **Attending Physician**, Northwestern Memorial Hospital (NMH), Chicago, IL
1987-1990 **Associate Director,** Midwest Regional Spinal Cord Care System, NUFSM/RIC/NMH
1990-1994 **Founder & Director**, Center for Stroke Rehabilitation, RIC, Chicago, IL
1991-1994 **Associate Professor**, PM&R, NUFSM
1993-2014 **Project Director**, Rehabilitation Research and Training Center on Stroke Rehabilitation, U.S. Department of Education, National Institute on Disability and Rehabilitation Research
1994- **Chairman**, Rehabilitation Medicine, Northwestern Memorial Hospital, Chicago, IL
1994-2007 **Senior Vice President and Medical Director**, Rehabilitation Institute of Chicago, Chicago, IL
1994- **Chairman**, Rehabilitation Medicine, Northwestern Memorial Hospital, Chicago, IL
1994- **The Paul B. Magnuson Professor and Chairman**, PM&R, NUFSM

2008- **Project Director**, Midwest Regional Traumatic Brain Injury Model System, RIC
2010-2012 **Interim Medical Director**, Brain Injury Medicine and Rehabilitation Program, RIC
2012-2017 **Medical Director**, Patient Recovery Unit, RIC
2017- **Co-Medical Director, Brain Innovation Center**, Shirley Ryan Abilitylab
2014- **Project Director**, Rehabilitation Research and Training Center on Health and Function for People with Physical Disabilities, U.S. Department of Education, National Institute on Disability and Rehabilitation Research

Other Experience and Professional Activities

1992- **Co-Editor in Chief**, *Topics in Stroke Rehabilitation*
1993 - **Editorial Board**, *Archives of Physical Medicine and Rehabilitation*
1993 -2009 **Editorial Board**, *American Journal of Physical Medicine and Rehabilitation*
1994 -2006 **Editorial Board**, *Journal of Neurological Rehabilitation*
1995 U.S. Patent No. 5397337 - Method and Apparatus for Artificially Stimulating Cough Reflex with Robert J. Jaeger, Ph.D.
2002-2003 **Member**, Technical Expert Panel to Develop Inpatient Rehabilitation Quality Measures
2010--2012 **Chairman**, Research Committee, American Academy of Physical Medicine and Rehabilitation
2012-- **Chairman**, Evidence-Based Practice Committee, American Academy of Physical Medicine and Rehabilitation

Honors

1992,96,00,06,08 Voted one of the Outstanding Physicians in Chicago by *Chicago Magazine*
1999-2000; 03; 06-07;10-18 Named one of the Best Physicians in Chicago by Castle-Connolley Publishers
2004 John W. Goldschmidt, MD Award for Excellence in Rehabilitation, National Rehabilitation Hospital, Washington, DC
2007 Elected to Alpha Omega Alpha Medical Honorary Society, NUFSM
2015 Distinguished Clinician Award, American Academy of Physical Medicine and Rehabilitation

C. Contributions to Science

1. Early in my academic career, my research focused on understanding the cognitive dysfunction that often accompanied a traumatic spinal cord injury. My colleagues and I were the first to describe the occurrence and the impact that these deficits on can have on rehabilitation outcomes. Cognitive functioning is associated with medical stability, the patient's ability to assimilate the necessary skills for survival and adaptation after spinal cord injury, and readmission patterns after discharge for initial inpatient rehabilitation.

a. Morris J, Roth E, Davidoff G. Mild closed head injury and cognitive deficits in spinal-cord-injured patients: incidence and impact. J Head Trauma Rehabil. 1986;1(2):31-42.
b. Davidoff G, Roth E, Morris J, Bleiberg J, Meyer PR. Assessment of closed head injury in trauma-related spinal cord injury. Paraplegia. 24:97-104; 1986.
c. Roth E, Davidoff G, Thomas P, Doljanac R, Dijkers M, Berent S, et al. A controlled study of neuropsychological deficits in acute spinal cord injury patients. Paraplegia. 27:480-489;1989.
d. Davidoff GN, Roth EJ, Richards JS. Cognitive deficits in spinal cord injury: epidemiology and outcome. Arch Phys Med Rehabil. 1992;73:275-284.

2. Another area of interest early in my academic and clinical career was in the course functional recovery after a neurological injury such as a spinal cord injury or stroke. Our research team examined how impairment related to functional outcomes and how this affected the course of rehabilitation. We also investigated how these factors influenced long-term community outcomes.

a. Yarkony GM, Roth EJ, Heinemann AW, Lovell L, Wu Y. Functional skills after spinal cord injury rehabilitation: three-year longitudinal follow-up. Archives of Physical Medicine and Rehabilitation. 1988;69:111-114.
b. Roth EJ, Lovell LL. Seven Year Trends in Stroke Rehabilitation: Patient Characteristics, Medical Complications, and Functional Outcomes. Topics in Stroke Rehabilitation. 2003;9(4):1-9.

c. Roth EJ. Lovell L. Community skill performance and its association with the ability to perform everyday tasks by stroke survivors one year following rehabilitation discharge. Topics in Stroke Rehabilitation. 2007;14(1):48-56. PMID: 17311790
d. Cramer SC, Wolf SL, Adams HP Jr, Chen D, Dromerick AW, Dunning K, Ellerbe C, Grande A, Janis S, Lansberg MG, Lazar RM, Palesch YY, Richards L, Roth E, Savitz SI, Wechsler LR, Wintermark M, Broderick JP. Stroke Recovery and Rehabilitation Research: Issues, Opportunities, and the National Institutes of Health StrokeNet. *Stroke*. 2017;48(3):813-819. PMID: 28826022

3. My clinical practice helped to inform several aspects of my research. One important area was on how medical complications and pre-existing comorbid conditions influenced the outcomes of patients during and after rehabilitation. I became especially interested in cardiopulmonary complications as these had tremendous impact on mortality and morbidity. Identifying clinical factors that are associated with increased risk of experiencing medical complications is valuable to facilitate the implementation of appropriate prevention and management interventions. These studies represent the impact of medical complications on outcomes.

a. Roth EJ. Lovell L. Harvey RL. Bode RK. Delay in transfer to inpatient stroke rehabilitation: the role of acute hospital medical complications and stroke characteristics. Topics in Stroke Rehabilitation. 2007;14(1):57-64. PMID: 17311791
b. Marciniak C, Korutz AW, Lin E, Roth E, Welty L, Lovell L. Examination of selected clinical factors and medication use as risk factors for pneumonia during stroke rehabilitation: a case-control study. American Journal of Physical Medicine and Rehabilitation. 2009;88(1):30-38. PMID: 19096289
c. Roth E, Stenson K, Powley S, Oken J, Primack S, Nussbaum S, Berkowitz M. Expiratory muscle training in spinal cord Injury: A randomized controlled trial. Arch Phys Med Rehabil. 91:857-861, 2010. PMID: 20510974
d. Pellicane AJ, Millis SR, Do KD, Temme KE, Sayyad A, Oswald MC, Roth EJ. The effect of protein and calorie intake on prealbumin, complications, length of stay, and function in the acute rehabilitation inpatient with stroke. NeuroRehabilitation. 33(3):367-76 2013. PMID: 23949068

4. Another area of research interest that has been heavily influenced by my clinical practice is in mobility and gait. Recovery of walking is a primary goal for patients after a stroke or spinal cord injury. For those patients for whom walking is not feasible, there is a compelling need to develop methods for improved mobility. I have been involved in investigating parameters such as amount and intensity of practice that appear to be contributors to improved function in patients post-stroke. I also have been involved in investigating and developing methods for mobility in patients who use wheelchairs.

a. Kim J, Park H, Bruce J, Rowles D, Holbrook J, Nardone B, West D, Laumann A, Roth E, Ghovanloo M. Assessment of the Tongue-Drive System using a Computer, a Smartphone, and a Powered-Wheelchair by People With Tetraplegia. IEEE Trans Neural Syst Rehabil Eng. 2016 26(1):68-78. PMID: 25730827
b. Hornby TG, Holleran CL, Leddy AL, Hennessy P, Leech KA, Connolly M, Moore JL, Straube D, Lovell L, Roth E. Feasibility of Focused Stepping Practice During Inpatient Rehabilitation Poststroke and Potential Contributions to Mobility Outcomes. Neurorehabil Neural Repair. 2015 Nov;29(10):923-32 PMID: 25721233
c. Hornby TG, Holleran CL, Hennessy PW, Leddy AL, Connolly M, Camardo J, Woodward J, Mahtani G, Lovell L, Roth EJ. Variable Intensive Early Walking Poststroke (VIEWS): A Randomized Controlled Trial. Neurorehabil Neural Repair 2016 Jun;30(5):440-50 PMID: 26338433
d. Hornby TG, Moore JL, Lovell L, Roth EJ. Influence of skill and exercise training parameters on locomotor recovery during stroke rehabilitation. Curr Opin Neurol. 2016;29(6):677-683. PMID: 27748688

D. Research Support

Active Research Support

90RT5027 (Roth) 10/1/14 – 09/30/19
NIDILRR, Administration for Community Living
Rehabilitation Research and Training Center on Developing Optimal Strategies in Exercise and Survival Skills to Increase Health and Function
The Center's projects will explore the role of motor priming and intensity of training to improve walking ability, determine the optimal dosing of intensive aphasia treatments, and develop a peer health navigator program that will improve the ability of people with disabilities to access community resources and the social environment. We will measure the economic and social value of each project.
Role: Principal Investigator and Center Director

5R01HD082216-02 (Wu) 8/6/15-7/30/20
NIH/NICHD
Date of Project Period:
Constraint induced movement therapy for walking in individuals post stroke
This project will test whether the efficacy of locomotor training will be improved through the application of constraint induced movement therapy to lower limb of individuals post-stroke during treadmill training.
Role: Co-Investigator

R01 (Roth/Kamper) 4/1/14-3/31/19
NIH
Altering Activation Patterns in the Distal Upper Extremity after Stroke
The goal of the proposed study is to explore the therapeutic benefit of a multimodality treatment combining the administration of a pharmacological agent for reducing unwanted neuromuscular hyperexcitability with a training paradigm focused on expanding exploration of the muscle activation workspace.
Role: Principal Investigator

16SDG30980033 (Suresh) 7/1/16-6/30/19
American Heart Association
Tracking the evolution of spasticity in acute stroke
The objective of this study is to track the time course of spasticity development in acute stroke survivors with experimental and clinical measures that would provide us with information regarding the neural source of reflex excitability.
Role: Investigator

4U10NS086608-04 (Prabhakaran) 9/30/13-7/31/18
NINDS
The Chicago Stroke Trials Consortium
Stroke Trials Network – Regional Coordinating Stroke Centers
Goal is to create a regional coordinating stroke center that will facilitate the execution of larger stroke clinical trials.
Role: Co-Investigator

U10NS077271-06 (Simuni) 9/1/11-6/30/25
NIH/NINDS
Clinical Research Sites for the Network of Excellence in Neuroscience Clinical Trials (NEXT Sites)
Participation in this network will enable us to contribute expertise and research subjects to neurological clinical trials and provide training for junior investigators to enable them to develop independent research careers.
Role: Co-Investigator

Spastic Paralysis Research Foundation of the Kiwanis of Illinois and Eastern Iowa (Roth) 10/1/97-9/30/18

Nutrition and Wellness in Persons with Stroke and Brain Injury

This is a series of studies on the role of nutrition in influencing outcomes after stroke or brain injury.
Role: Principal Investigator

Completed Research Support

H133B080031 (Roth) 10/01/08 – 09/30/14
NIDRR, Department of Education

Rehabilitation Research and Training Center on Enhancing the Functional and Employment Outcomes of Individuals Who Experience a Stroke

Purpose of this project is to develop and evaluate technology and programs designed to assist stroke survivors in community participation and vocation.
Role: Principal Investigator and Director

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Linda Weil Foster

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Research Coordinator

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Start Date MM/YYYY	Completion Date MM/YYYY	FIELD OF STUDY
Tulane University, New Orleans, LA	BS		06/1985	Psychology
Duke University, Durham, NC	MS		05/1987	Physical Therapy

A. Personal Statement

Because of my experience in clinical care and research, as well as my management experience, I am well suited to participate in this research project. Throughout my professional career, I have worked extensively with stroke patients, many with aphasia. From 2008-2010, I conducted a research study with stroke survivors utilizing a robotic device called the KineAssist. I currently treat outpatients, primarily stroke survivors, utilizing the KineAssist for physical therapy treatment. From 2014-2016, I was involved in a study funded by the Patient-Centered Outcomes Research Institute (PCORI) and titled “Developing Quality Metrics from Patient-Reported Outcomes”. For this study, I had the opportunity to work closely with Dr. Heinemann. The study was conducted at both the Shirley Ryan AbilityLab (formerly Rehabilitation Institute of Chicago) and the Alexian Brothers Rehabilitation Hospital and involved enrolling and evaluating patients with a neurological diagnosis. My role in the current study will be similar to that of the PCORI study. With the research speech and language pathologist, I will supervise the research assistant assigned to the Alexian Brothers Rehabilitation Hospital, to ensure that recruitment goals are met and quality data obtained.

B. Positions and Honors

Positions and Employment

1987-1992 Physical Therapist, Medical College of Virginia Hospitals, Richmond Virginia
1992-1998 Senior Physical Therapist, Rehabilitation Institute of Chicago, Chicago IL
1998-2004 Allied Health Manager, Rehabilitation Institute of Chicago, Chicago IL
2004-2008 Clinical Manager, Day Rehabilitation, Rehabilitation Institute of Chicago at Alexian Brothers, Elk Grove Village, IL
2008-Present Research Coordinator, Shirley Ryan AbilityLab/Rehabilitation Institute of Chicago at Alexian Brothers Rehabilitation Hospital, Elk Grove Village, IL

Other Experience and Professional Memberships

1985-Present Member, American Physical Therapy Association
1992-Present Member, Illinois Physical Therapy Association

C. Contribution to Science

1. Heinemann, A.W., Deutsch, A., Cella, D., Cook, K.F., Foster, L., Miskovic, A., Davis, K., & Goldsmith, A. Feasibility of Collecting Patient-Reported Outcomes for Inpatient Rehabilitation Quality Reporting. *Health Services Research Journal*. 15 JUN 2017, DOI: 10.1111/1475-6773.12729
2. Schalet, B., Kallen, M., Heinemann, A.W., Deutsch, A., Cook, K. F., Foster, L., Cella, D. Using PROMIS Pain Interference Items to Improve Quality Measurement in Inpatient Rehabilitation Facilities. *JAMDA.* (2018)

For the PCORI project I was the site co-investigator and liaison for the Alexian Brothers Rehabilitation Hospital. My responsibilities included assisting in subject recruitment, research coordination, and dissemination of research results.
Summary of PCORI results:

- Collection of patient-reported outcome measures (PROMS) during and after an IRF (Inpatient Rehabilitation Facility) stay from persons with neurological disorders is feasible
- A substantial proportion of patients require assistance
- The majority of patients could use a tablet computer and were willing to complete the survey one-month after discharge
- Multiple reminders and telephone interviews were required for follow up surveys; results would be biased without research follow-up efforts

Conclusions:

- Collection of patient-reported data while still in hospital results in a higher response rate
- Most follow-up response differences are more favorable

D. Research Support

Ongoing Research Support
None

Completed Research Support
CD12-11-4201 (PCORI) Heinemann (PI) 09/01/2013-08/31/2016
Developing Quality Metrics from Patient-Reported Outcomes for Medical Rehabilitation
Goals of the project were:

1. to identify issues that are important to the quality of care for rehabilitation patients that are amenable to the collection of patient-reported outcomes (PROMS)
2. evaluate the feasibility of collecting PROMS
3. specify items required for quality measure development and design data collection modules that can be used in quality improvement efforts and to demonstrate accountability of health care delivery

BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Allan J. Kozlowski, PhD

eRA COMMONS USER NAME (credential, e.g., agency login): [redacted]

POSITION TITLE: Assistant Professor, Department of Epidemiology and Biostatistics, Michigan State University College of Human Medicine; and Director of Outcomes Research at Mary Free Bed Rehabilitation Hospital

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of British Columbia, Vancouver CAN	B.Sc. (PT)	06/1991	Physical Therapy
University of British Columbia, Vancouver CAN	PhD	11/2010	Rehabilitation Sciences
Rehabilitation Institute of Chicago, Chicago USA		09/2012	Postdoctoral Fellowship

A. Personal Statement

I have the expertise, knowledge, skill, and access to resources necessary to successfully carry out my roles as described in the proposed research project. In regard to my role as Site PI at Mary Free Bed Rehabilitation Hospital, I have lead or co-authored seven manuscripts and co-instructed courses on topics of longitudinal modeling. As PI or co-Investigator on several Department-, State-, and private foundation-funded grants, I am familiar with the regulatory and procedural requirements of implementing human subjects' research. In regard to my role as data analyst, I have the knowledge, skill, and experience required to perform the required data analyses, including longitudinal methods that model outcomes as trajectories. I am familiar with measurement issues related to the primary and secondary outcome measures, and covariates including biomarkers. I have established relationships with the senior researchers on this proposal. Over the past eight years collaborated and published with Allen W. Heinemann, PhD, and have a collegial relationship established over the past seven years with Leora Cherney, PhD, CCC-SLP.

1. **Kozlowski AJ**, Heinemann AW. Using individual growth curve models to predict recovery and activities of daily living after spinal cord injury: an SCIRehab project study. Arch Phys Med Rehabil. 2013 Apr;94(4 Suppl):S154-64.e1-4. PubMed PMID: 23527771.

2. **Kozlowski AJ**, Singh R, Victorson D, Miskovic A, Lai JS, Harvey RL, Cella D, Heinemann AW. Agreement Between Responses From Community-Dwelling Persons With Stroke and Their Proxies on the NIH Neurological Quality of Life (Neuro-QoL) Short Forms. Arch Phys Med Rehabil. 2015 Nov;96(11):1986-92.e14. Epub 2015 Jul 21. PubMed PMID: 26209471; PubMed Central PMCID: PMC4628567.

3. **Kozlowski AJ**, Cella D, Nitsch KP, Heinemann AW. Evaluating Individual Change With the Quality of Life in Neurological Disorders (Neuro-QoL) Short Forms. Arch Phys Med Rehabil. 2016 Apr;97(4):650-4.e8. Epub 2015 Dec 29. PubMed PMID: 26740062; PubMed Central PMCID: PMC4994512.

4. **Kozlowski AJ**, Frank H, Miriam LL, Sandra M, Susan G, et al. Effect of exoskeleton-assisted locomotor training on recovery rate of motor functioning for inpatients with stroke compared to historical controls. Phys Ther. Forthcoming; Under review.

B. Positions and Honors

Positions and Employment

1991-1997 Physical Therapist, Workers' Compensation Board of British Columbia, Richmond, Canada
1997-2003 Rehabilitation Manager, Workers' Compensation Board of British Columbia, Richmond, Canada
2004-2010 Pre-doctoral Candidate, Rehabilitation Research Training Programs, Faculty of Medicine, University of British Columbia, Vancouver, Canada
2005-2010 Clinical Instructor (Contract): "RSPT514 Clinical Practice I", Department of Physical Therapy, University of British Columbia, Vancouver BC, Canada
2010 Physical Therapist (contract), CBI Rehabilitation, Burnaby BC, Canada
2010-2013 Fellow, Center for Rehabilitation Outcomes Research, Rehabilitation Institute of Chicago, and the Center for Healthcare Studies, Feinberg Medical School, Northwestern University, Chicago IL
2011-2013 Instructor (Contract): "RHSC505 Measurement for Assessment, Planning, and Evaluation", Online Master of Rehabilitation Science Program, University of British Columbia, Vancouver BC, Canada
2012 Course Developer (Contract): "RHSC505 Measurement for Assessment, Planning, and Evaluation", Online Master of Rehabilitation Science Program, University of British Columbia, Vancouver, Canada
2012 Adjunct Faculty (Contract Instructor): "OT410 Research Methods", Department of Occupational Therapy, University of Illinois at Chicago, Chicago IL
2013-2016 Assistant Professor, Department of Rehabilitation Medicine, Icahn School of Medicine at Mount Sinai, New York, NY
2016-Present Assistant Professor, Department of Epidemiology and Biostatistics, Michigan State University, Grand Rapids, MI; and Director of Outcomes Research, Mary Free Bed Rehabilitation Hospital, Grand Rapids, MI

Committee Service

1992-1994 Board Member, Association of Physiotherapists and Massage Practitioners of British Columbia
1994-1997 Board Member, College of Physical Therapists of British Columbia
1994-1995 Chair, Code of Ethics Development Committee, College of Physical Therapists of British Columbia
1994-1997 Chair, Patient Relations Committee, College of Physical Therapists of British Columbia
1996-1997 Investigator, Inquiry Committee, College of Physical Therapists of British Columbia
2004-2007 Department Representative, Graduate Student Society, University of British Columbia
2006-2007 Chair, Oversight Committee, Graduate Student Society, University of British Columbia
2006-2007 Member, Back Strain Task Force, Physiotherapy Association of British Columbia
2007-2008 Graduate Student Representative, Department Head Search Committee, Department of Physical Therapy, University of British Columbia (UBC)
2010 Member, "Physician's Briefings: Work Related Disorders" Development Committee, Physiotherapy Association of British Columbia
2012-2014 Member, American Congress of Rehabilitation Medicine, (ACRM) Measurement Networking Group
2013-Present Member, ACRM, Spinal Cord Injury Interdisciplinary Special Interest Group, Member
2014-Present Secretary, ACRM, Spinal Cord Injury Measurement Networking Group

Professional Memberships

1987-2010 Physiotherapy Association of British Columbia (PABC)
1987-Present Canadian Physiotherapy Association (CPA), Membership Number 15211
1991-Present College of Physical Therapists of British Columbia (CPTBC), Reg. 02686 (Inactive as of January 2011)
2004-Present American Physical Therapy Association (APTA), Membership Number 166155

Other Professional Activities

2010-Present Manuscript Reviewer, *Archives of Physical Medicine and Rehabilitation*
2014 Grant reviewer, Rick Hansen Institute

2014-Present Manuscript Reviewer, *PM&R* journal
2014-2015 Special Issue Guest Editor, *Topics in Spinal Cord Injury Rehabilitation*
2015 Grant reviewer, National Multiple Sclerosis Society
2015-Present Manuscript Reviewer, *Journal of the Peripheral Nervous System*

C. Contribution to Science

1. Longitudinal Modeling. My most significant contribution has been in demonstrating and promoting the use of longitudinal analytic methods, including trend analysis and individual growth curve modeling, to rehabilitation science and practice. Unlike many clinical and research outcomes, most rehabilitation results are not well represented as a dichotomy or simple change in status, but rather evolve in a predictable pattern over a period of time, which may span multiple interventions. Trend analyses facilitate modeling of best-fit trajectories while IGC analyses explain individual variance around the trajectory parameters. Trend analyses permit the comparison of recovery rates as an outcome, and thus are suited to examining treatment effects provided during recovery in randomized controlled trials. IGC methods can construct individual trajectories, which have the prognostic potential, and thus could improve treatment planning and clinical decision-making. In addition to previously cited works, also see

a. Pretz CR, **Kozlowski AJ**, Chen Y, Charlifue S, Heinemann AW. Trajectories of Life Satisfaction following Spinal Cord Injury. Archives of Physical Medicine and Rehabilitation. Forthcoming; In press.

b. Hart T, **Kozlowski AJ**, Whyte J, Poulsen I, Kristensen K, Nordenbo A, Heinemann AW. Functional recovery after severe traumatic brain injury: an individual growth curve approach. Arch Phys Med Rehabil. 2014 Nov;95(11):2103-10. Epub 2014 Jul 7. PubMed PMID: 25010537.

c. Kozlowski AJ, Hyland F, Ludwig ML, Marrone S, Golden S, Yensr N et al. Prototype individual growth model for inpatient recovery of motor function in persons recovering from stroke. Phys Ther 2017;Under Review.

2. Measurement and psychometrics. Another significant contribution lies in works to evaluate measurement accuracy and precision of new and existing rehabilitation outcome measurement instruments, and to facilitate clinical application of such instruments. Instrument validation is an ongoing, context-specific endeavor, which facilitates research applications. However, clinical application of an instrument requires the ability to interpret change for individual patients, which is not always possibly from published research results. Although recently published, the article listed in my personal statement in interpreting individual change on the Neuro-QoL short forms has generated positive feedback. In addition to previously cited works, also see

a. Pretz CR, Kean J, Heinemann AW, **Kozlowski AJ**, Bode RK, Gebhardt E. A Multidimensional Rasch Analysis of the Functional Independence Measure Based on the National Institute on Disability, Independent Living, and Rehabilitation Research Traumatic Brain Injury Model Systems National Database. J Neurotrauma. 2016 Jul 15;33(14):1358-62. Epub 2016 Jan 28. PubMed PMID: 26559881.

b. Pretz CR, **Kozlowski AJ**, Charlifue S, Chen Y, Heinemann AW. Using Rasch motor FIM individual growth curves to inform clinical decisions for persons with paraplegia. Spinal Cord. 2014 Sep;52(9):671-6. Epub 2014 Jun 17. PubMed PMID: 24937699.

c. Bode RK, Heinemann AW, **Kozlowski AJ**, Pretz CR. Self-scoring templates for motor and cognitive subscales of the FIM instrument for persons with spinal cord injury. Arch Phys Med Rehabil. 2014 Apr;95(4):676-679.e5. Epub 2013 Dec 3. PubMed PMID: 24309071.

3. Exoskeleton Feasibility and Safety. I have also provided a significant contribution to the emerging literature on powered exoskeleton applications. In addition to the articles cited below, I have two manuscripts in preparation from a pilot project to test the feasibility and safety of a powered exoskeleton by persons with multiple sclerosis. To our knowledge, this study was the first to test an exoskeleton with persons with MS.

a. Kozlowski AJ, Bryce TN, Dijkers MP. Time and effort required by persons with spinal cord injury to learn to use a powered exoskeleton for assisted walking. Top Spinal Cord Injury Rehabil. Top Spinal Cord Inj Rehabil. 2015 April 24; In 21(2):110-21.

b. Bryce TN, Dijkers MP, **Kozlowski AJ**. Framework for Assessment of the Usability of Lower-Extremity Robotic Exoskeletal Orthoses. Am J Phys Med Rehabil. 2015 Nov;94(11):1000-14. PubMed PMID: 26098923.

c. Kozlowski AJ, Fabian M, Lad D, Delgado A. Feasibility and safety of a powered exoskeleton for assisted walking for persons with multiple sclerosis: a single-group preliminary study. Arch Phys Med Rehabil. 2017; under review.

d. Delgado A, Lad D, Fabian M, **Kozlowski AJ**. A Cross-Sectional Study on the Metabolic and Physiological Responses to Exoskeleton-2 Assisted Walking for Persons with Multiple Sclerosis. Arch Phys Med Rehabil. 2017; under review.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/1FAZBdTNHbUkE/bibliography/47391004/public/?sort=date&direction=ascending

D. Research Support

ON GOING RESEARCH SUPPORT
None

COMPLETED RESEARCH SUPPORT IN LAST 3 YEARS

1. **Title:** Feasibility and utility of routine exoskeleton walking.
   Role: PI**. Funding Agency:** Department of Rehabilitation Medicine Development Fund (anonymous donations collected with assistance of Mount Sinai's Development Office).
   Grant #: Not Applicable.
   Funding period: 09/01/2013 – 08/31/2015.
   Project Goal: Test the safety and feasibility of a powered lower extremity exoskeleton for persons with spinal cord injury.

2. **Title:** Ekso Wearable Robotic Walking System for Persons with SCI.
   Role: PI. **Funding Agency:** Craig H. Neilsen Foundation – Quality of Life.
   Grant #: 250542.
   Funding period: 07/01/2013 – 06/30/2014.
   Project Goal: Fund purchase of a powered lower extremity exoskeleton for spinal cord injury research.

3. **Title:** Mount Sinai Spinal Cord Injury Research Program Shared Equipment and Bridge Funding.
   Role: Co-Investigator (PI: Marcel Dijkers, PhD).
   Funding Agency: New York State Department of Health and the Spinal Cord Injury Research Board.
   Grant #: C029126.
   Funding period: 10/01/2013 – 02/28/2014.
   Project Goal: Fund purchase of equipment for spinal cord injury research.

4. **Title:** Modeling Functional Outcome from Spinal Cord Injury and Traumatic Brain Injury Model Systems Databases with Individual Growth Methods.
   Role: Sub-Investigator (PI: Ken Ottenbacher, PhD).
   Funding Agency: NIH.
   Grant #: R24-HD065702.
   Funding period: 10/01/2013 – 02/28/2014.
   Project Goal: Fund effort and training for modeling of rehabilitation outcomes for persons with spinal cord injury or traumatic brain injury as trajectories.

5. **Title:** Rehabilitation Robotics Research Program Research Assistant Funding.
   Role: PI.
   Funding Agency: Peter Jay Sharp Foundation.
   Grant #: Not Applicable.
   Funding period: 07/01/2014 – 06/30/2015.
   Project Goal: Fund effort for a Research Assistant.

6. **Title:** Expanding capacity for multi-site SCI research.
   Role: PI.
   Funding Agency: New York State Department of Health and the Spinal Cord Injury Research Board.
   Grant #: C030090.
   Funding period: 10/01/2014 – 02/28/2015.
   Project Goal: Fund effort for research personnel and purchase of equipment for spinal cord injury research.

7. **Title:** Spinal Cord Injury Research Institutional Support.
   Role: PI.
   Funding Agency: New York State Department of Health and the Spinal Cord Injury Research Board.
   Grant #: C030171
   Funding period: 12/01/2014 – 03/31/2015.
   Project Goal: Fund effort for research personnel and purchase of equipment for spinal cord injury research.

8. **Title:** Feasibility of the ReWalk™ exoskeleton-assisted walking for persons with multiple sclerosis.
   Role: PI.
   Funding Agency: National Multiple Sclerosis Society.
   Grant #: PP3359.
   Funding period: 01/01/2015 – 12/31/2015.
   Project Goal: Test the safety and feasibility of a powered lower extremity exoskeleton for persons with multiple sclerosis.

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Allen		Heinemann	Ph.D	PD/PI	[redacted]	3.00			[redacted]	[redacted]	[redacted]
2 .	Dr.	Leora		Cherney	PhD	PD/PI	[redacted]	3.00			[redacted]	[redacted]	[redacted]
3 .	Dr.	Elliot		Roth		Co-Investigator	[redacted]	0.24			[redacted]	[redacted]	[redacted]
4 .	Dr.	Marwan		Baliki	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]
5 .	Dr.	Andrea		Domenighetti	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]
6 .	Dr.	Linda		Foster	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	SLP	6.00			[redacted]	[redacted]	[redacted]
1	Project Manager	6.00			[redacted]	[redacted]	[redacted]
1	Research Assistant	12.00			[redacted]	[redacted]	[redacted]
1	Research Assistant	6.00			[redacted]	[redacted]	[redacted]
4	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	[redacted]
2. Foreign Travel Costs	
Total Travel Cost	[redacted]

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period:** 1

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	[redacted]
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	[redacted]
6. Equipment or Facility Rental/User Fees	[redacted]
7. Alterations and Renovations	
8 . Subject Reimbursement	[redacted]
Total Other Direct Costs	[redacted]

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number) HHS, Arif Karim [redacted]

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1234-Heinemann_BudgetJust_Final.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ● Subaward/Consortium

Enter name of Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period:** 2

A. Senior/Key Person.

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1. Dr.	Allen		Heinemann	Ph.D	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]
2. Dr.	Leora		Cherney	PhD	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]
3. Dr.	Elliot		Roth		Co-Investigator	[redacted]	0.24.			[redacted]	[redacted]	[redacted]
4. Dr.	Marwan		Baliki	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]
5. Dr.	Andrea		Domenighetti	PhD	Co-Investigator	[redacted]	1.20.			[redacted]	[redacted]	[redacted]
6. Dr.	Linda		Foster	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel.

Number of Personnel*.	Project Role*.	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	SLP	6.00			[redacted]	[redacted]	[redacted]
1	Project.Manager.	6.00			[redacted]	[redacted]	[redacted]
1	Research Assistant	12.00			[redacted]	[redacted]	[redacted]
1	Research Assistant	6.00			[redacted]	[redacted]	[redacted]
1	Research Associate	0.60			[redacted]	[redacted]	[redacted]
5	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]

Total Salary, Wages and Fringe Benefits (A+B) [redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000+04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	[redacted]
2. Foreign Travel Costs	
Total Travel Cost	[redacted]

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period:** 2

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	[redacted]
2. Publication Costs	[redacted]
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	[redacted]
6. Equipment or Facility Rental/User Fees	[redacted]
7. Alterations and Renovations	
8 . Subject Reimbursement	[redacted]
Total Other Direct Costs	[redacted]

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1234-Heinemann_BudgetJust_Final.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2021 **End Date*:** 03-31-2022 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Allen		Heinemann	Ph.D	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]
2 .	Dr.	Leora		Cherney	PhD	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]
3 .	Dr.	Elliot		Roth		Co-Investigator	[redacted]	0.24			[redacted]	[redacted]	[redacted]
4 .	Dr.	Marwan		Baliki	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]
5 .	Dr.	Andrea		Domenighetti	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]
6 .	Dr.	Linda		Foster	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person **144,685.00**

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	SLP	6.00			[redacted]	[redacted]	[redacted]
1	Project Manager	6.00			[redacted]	[redacted]	[redacted]
1	Research Assistant	12.00			[redacted]	[redacted]	[redacted]
1	Research Assistant	6.00			[redacted]	[redacted]	[redacted]
1	Research Associate	0.60			[redacted]	[redacted]	[redacted]
5	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2021 **End Date*:** 03-31-2022 **Budget Period:** 3

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	[redacted]
2. Foreign Travel Costs	
Total Travel Cost	[redacted]

E. Participant/Trainee Support Costs		Funds Requested ($)*
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2021 **End Date*:** 03-31-2022 **Budget Period:** 3

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	[redacted]
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	[redacted]
6. Equipment or Facility Rental/User Fees	[redacted]
7. Alterations and Renovations	
8 . Subject Reimbursement	[redacted]
Total Other Direct Costs	[redacted]

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1234-Heinemann_BudgetJust_Final.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Enter name of Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period: 4**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Allen		Heinemann	Ph.D	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]
2 .	Dr.	Leora		Cherney	PhD	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]
3 .	Dr.	Elliot		Roth		Co-Investigator	[redacted]	0.24			[redacted]	[redacted]	[redacted]
4 .	Dr.	Marwan		Baliki	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]
5 .	Dr.	Andrea		Domenighetti	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]
6 .	Dr.	Linda		Foster	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	SLP	6.00			[redacted]	[redacted]	[redacted]
1	Project Manager	6.00			[redacted]	[redacted]	[redacted]
1	Research Assistant	12.00			[redacted]	[redacted]	[redacted]
1	Research Assistant	6.00			[redacted]	[redacted]	[redacted]
1	Research Associate	0.60			[redacted]	[redacted]	[redacted]
5	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period:** 4

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	[redacted]
2. Foreign Travel Costs	
Total Travel Cost	[redacted]

E. Participant/Trainee Support Costs		Funds Requested ($)*
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period:** 4

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	[redacted]
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	[redacted]
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . Subject Reimbursement	[redacted]
Total Other Direct Costs	[redacted]

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1234-Heinemann_BudgetJust_Final.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ● Subaward/Consortium

Enter name of Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period:** 5

A. Senior/Key Person.

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1. Dr.	Allen		Heinemann	Ph.D	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]
2. Dr.	Leora		Cherney	PhD	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]
3. Dr.	Elliot		Roth		Co-Investigator	[redacted]	0.24			[redacted]	[redacted]	[redacted]
4. Dr.	Marwan		Baliki	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]
5. Dr.	Andrea		Domenighetti	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]
6. Dr.	Linda		Foster	PhD	Co-Investigator	[redacted]	1.20			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel.

Number of Personnel*.	Project Role*.	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	SLP	6.00			[redacted]	[redacted]	[redacted]
1	Project.Manager.	6.00			[redacted]	[redacted]	[redacted]
1	Research Assistant	12.00			[redacted]	[redacted]	[redacted]
1	Research Assistant	6.00			[redacted]	[redacted]	[redacted]
1	Research Associate	0.60			[redacted]	[redacted]	[redacted]
5	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]

Total Salary, Wages and Fringe Benefits (A+B) [redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000+04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ● Subaward/Consortium

Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period:** 5

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	[redacted]
2. Foreign Travel Costs	
Total Travel Cost	[redacted]

E. Participant/Trainee Support Costs	**Funds Requested ($)***
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	
Number of Participants/Trainees **Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ○ Subaward/Consortium

Organization: Rehabilitation Institute of Chgo dba Shirley Ryan AbilityLab

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
1. Materials and Supplies	[redacted]
2. Publication Costs	[redacted]
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	[redacted]
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8 . Subject Reimbursement	[redacted]
Total Other Direct Costs	[redacted]

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1234-Heinemann_BudgetJust_Final.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

Budget Justification
Shirley Ryan AbilityLab (formerly the Rehabilitation Institute of Chicago)

Personnel

Table 1: RIC Personnel Allocation (Calendar Months)						
Personnel	**Role**	**Year 1**	**Year 2**	**Year 3**	**Year 4**	**Year 5**
Allen Heinemann	Co-Principal Investigator	3.00	2.40	2.40	2.40	2.40
Leora Cherney	Co-Principal Investigator	3.00	2.40	2.40	2.40	2.40
Elliot Roth	Co-Investigator	0.24	0.24	0.24	0.24	0.24
Linda Foster	Co-Investigator	1.20	1.20	1.20	1.20	1.20
Andrea Domenighetti	Co-Investigator	1.20	1.20	1.20	1.20	1.20
Marwan Baliki	Co-Investigator	1.20	1.20	1.20	1.20	1.20
TBD	Project Manager	6.00	6.00	6.00	6.00	6.00
Rajeswari Pichika	Research Associate		0.60	0.60	0.60	0.60
TBD	Research Assistant	12.00	12.00	12.00	12.00	12.00
TBD	Research Assistant	6.00	6.00	6.00	6.00	6.00
Rosalind Hurwitz	Speech Language Pathologist	6.00	6.00	6.00	6.00	6.00

Allen Heinemann, PhD, PD/PI, 3 CAL in Y1 when the grant is starting up and 2.4 CAL in Y2-Y5. As the Director of the Center for Rehabilitation Outcomes Research, Dr. Heinemann has over 25 years of experience in outcomes research and will provide scientific leadership to ensure fulfillment of the programmatic, fiscal, and reporting requirements of this project. In addition, he will oversee the project manager and data analyst.

Leora R. Cherney, PhD, PD/PI, 3 CAL in Y1 when the grant is starting up and 2.4 calendar months Y2-Y5. Dr. Cherney is the Scientific Chair, Think & Speak at the SRALab and the Director of the Center for Aphasia Research and Treatment. She has over 30 years of experience in adult neurologic communication disorders, with an emphasis on treatment research in persons with aphasia. She will provide scientific and fiscal leadership in all aspects of the project, and specifically will oversee the speech-language pathologist and research assistants relative to data collection from participants with aphasia.

Elliot Roth, MD, Co-Investigator, 0.24 CAL months in each of Y1-Y5. Dr. Roth is the Chair of the Department of Physical Medicine & Rehabilitation at Northwestern University's Feinberg School of Medicine and an attending at the SRALab. His primary role will be to provide expertise in stroke rehabilitation including assistance with determining subject eligibility and review of clinical MRI scans.

Linda Foster, MS, Co-Investigator, will serve as site PI at ABRH at 1.20 CAL in Y1-Y5. As a Physical Therapist and researcher who has significant experience with the stroke population, she will work with the research speech-language pathologist to oversee the site research assistant in recruitment and data collection.

Andrea Domenighetti, PhD, Co-Investigator, an Investigator in the Biologics Lab at SRALab will oversee the genomics aspect of the project. He will devote 1.20 CAL months in Y1-Y5. He will also work closely with **Rajeswari Pichika PhD**, who will conduct the actual assays in Y2 and Y4. Their expertise is in biochemical and molecular properties of muscle and they are investigating novel methods of cell culture assays in stroke. **Dr. Domenighetti,** will participate in publication and dissemination of study results including abstracts, presentations, and manuscripts that arise from this work.

Rajeswari Pichika, PhD., Research Associate in the Biologics Lab at the SRALab will conduct the assays in under the direction of Dr. Domenighetti. She will devote 0.60 CAL months in Y2-Y5.

Marwan Baliki, PhD, Co-**Investigator,** will oversee the imaging aspects of the project, including the conduct and interpretation of the resting state and anatomical scans obtained from SRALab participants. He also will review clinical scans from participants at the ABRH and MFRH sites to determine lesion size and location. Dr.

Baliki has expertise in state of the art brain imaging technology. He will devote 1.20 CAL months in Y1-Y5. He will participate in publication and dissemination of study results including abstracts, presentations, and manuscripts that arise from this work.

TBD Project Manager, will devote 6 CAL months effort in Y1-Y5 to overseeing day-to-day project operations across sites. He will organize project meetings to facilitate project aims and requirements, ensure data collection (including saliva samples) and documentation consistency across sites, monitor project enrollment, and schedule rs-fMRIs at the SRALab. Together with the research speech-language pathologist, he will supervise the SRALab's research assistants.

Rosalind Hurwitz, MA CCC-SLP, Research Speech-Language Pathologist has over ten years' experience in the Center for Aphasia Research and Treatment at the SRALab where her primary responsibility has been as a "blind" assessor in various clinical trials. In this project, she will devote 6 CAL months effort in Y1-Y5 to train the site PIs, project manager and research assistants in supported communication techniques for aphasia. She will also train the research assistants in the administration of the assessment battery, periodically observe them to ensure consistency, and rescore a portion of the assessments (at least 10%) to ensure reliability.

TBD, Research Assistant, will devote 12 CAL months effort in Y1-Y5 to recruitment, screening potential participants, obtaining informed consent, and executing data collection activities at the SRALab (formerly the Rehabilitation Institute of Chicago) under the direction of the research speech-language pathologist. She also will be responsible for making monthly phone calls to participants to review their participation in any outpatient therapy, aphasia conversation groups, or other communication-focused activities. She will be responsible for maintaining accurate organization and record of all study activities, under the direction of the project manager.

TBD, Research Assistant, will devote 6 calendar months effort in Y1-Y5 to recruitment, screening potential participants, obtaining informed consent, and executing data collection activities at ABRH under the direction of the research speech-language pathologist. She also will be responsible for making monthly phone calls to participants to review their participation in any outpatient therapy, aphasia conversation groups, or other communication-focused activities. She will be responsible for maintaining accurate organization and record of all study activities, under the direction of the project manager.

Fringe benefits
RIC's fringe benefits are calculated at DHHS approved rate: [redacted]%. [redacted]% inflation rate is used for all salary calculations.

Travel
Travel expenses are budgeted for the Co-Principal Investigators (and others as appropriate) to disseminate study findings during Y1-Y5 (2 meetings per year at [redacted] per meeting in Y1-Y4; 4 meetings in Y5; Total for 5 years = [redacted]). Expenses cover conference fees, airline fares, hotel, ground transportation, and *per diem* expenses. Ground travel will be by automobile and reimbursed at the rate allowed by the IRS; economy airfare charges and the General Services Administration-allowed per diem rates are used. Travel expenses will be reimbursed in accordance with SRALab policy.

Other Direct Costs
Office Supplies [redacted]
Office supplies are budgeted at [redacted] for Y1. Y1 will cover expenses associated with project start-up including binders for the study protocol and standard operating procedures, paper to print fliers and test forms, and other general office supplies. An additional $[redacted] is budgeted over Y2-Y5 to cover printing and test form needs.

Computer Software (iPad Neuro-QoL Application, SPSS Base/Advanced/Regression Statistics Package, Mplus Base Program/Combination Add-On and Winsteps) [redacted]
).

A total of [redacted] is budgeted for software. In Year 1, the Connors Continuous Performance Test – 3 software [redacted] each for a total of [redacted]) will need to be purchased for ABRH and MFRH. The SRALab already has one for use there. We also budgeted [redacted] per year for licensing for the iPad Toolbox Application which will be required for the computer adapted administration of the Neuro-QoL item banks. SPSS, Mplus, and Winsteps licenses will be required for data analysis. We have budgeted SPSS licenses at [redacted] each beginning in Y2 for the Data Analyst and Y3 for the PI. Mplus and Winsteps require a one-time fee of [redacted] and [redacted] respectively. We will purchase Mplus and Winsteps licenses for Data Analyst in Y1 and Co-Investigator Kozlowski in Y2.

Lab Equipment ($[redacted])
Data collection requires [redacted] of equipment during Y1. Each site will require a Western Aphasia Battery-Revised [redacted] to be purchased in Y1 with replenishment of forms in subsequent years. Other behavioral assessments will need to be photocopied and are included under office supplies.
In Y1, each site will also require an iPad with accommodation accessories [redacted]) for the NeuroqoL administration.

The research assistant at each site will be provided with a **videocamera and tripod** so that every assessment can be recorded for later review as needed. We estimate the cost of this equipment to be [redacted] per site for a total of [redacted] in Y1.

DNA Saliva Test Kits have been budgeted at [redacted] We expect that saliva collection will occur on all subjects at the start of their participation in the project and prior to any drop-out. These funds are distributed through Y1-Y3.

Radiology services [redacted])
We estimate that the resting state fMRI costs will be [redacted] per participant for an estimated [redacted] participants. Research radiology costs at the SRALab are offered at a reduced rate of [redacted] per [redacted] minutes of scanning time.

Publication Costs [redacted]
By the end of Y2, we expect to submit publications to peer-reviewed journals. Dissemination will continue through the end of the project with an expected total budget of [redacted] to cover open access fees.

Subject Reimbursement ($[redacted] Y1-Y5)
We will recruit 400 participants with a first admission due to stroke and aphasia and admitted to one of the 3 data collection facilities during Y1-Y3. We will over-recruit to account for 15% attrition at 6 months and another 10% attrition at the 18-month data collection time points. Each site will recruit 100 participants with complete data across all time points. Participants will receive [redacted] after the inpatient rehabilitation discharge assessment. The honorarium will increase to [redacted] for the 6-month visit, [redacted] for the 12-month visit, and [redacted] for the 18-month follow-up. Therefore, those completing all assessments will receive a total of [redacted] which is budgeted at a total of [redacted]. An additional [redacted] is budgeted for those subjects who do not complete all assessments. The honorarium covers subjects' time, energy, and transportation costs.

Indirect Costs
F&A has been calculated based on the following DHHS approved rates:

- [redacted] MTDC Beginning 09/01/18 – 08/31/20 and thereafter- Provisional

Mary Free Bed Rehabilitation Hospital
Defining Trajectories of Linguistic, Cognitive-Communicative and Quality of Life Outcomes in Aphasia

Personnel

Allan J. Kozlowski PhD, Site Principal Investigator (2.4 CAL months for Years 1-5)
Dr. Kozlowski is contracted from Michigan State University – College of Human Medicine, Department of Epidemiology and Biostatistics, to be the Director of Outcomes Research at Mary Free Bed Rehabilitation Hospital (MFBRH). As Site PI he will oversee the administration and operations of the Mary Free Bed site and coordinate the communication, interactions and data sharing with the research team at Shirley Ryan AbilityLab. Dr. Kozlowski will play a major role in statistical analysis and data interpretation. He will also participate in administrative meetings. (Dr. Kozlowski's salary is contracted directly from Michigan State University)

John F. Butzer MD, Site Senior Advisor (0.6 CAL months for Years 1-5)
Dr. Butzer is the Director of Research at MFBRH. As a senior manager at MFBRH he will oversee the personnel and address institutional concerns arising from site administration and operations. Dr. Butzer will advise Dr. Kozlowski on institutional and staffing issues. He will also participate in administrative meetings.

TBD, Research Assistant (6 CAL months for Years 1 & 5; 12 CAL months for Years 2-4)
The research assistant will report directly to Ms. Virva, the Site Coordinator, to assist with the engagement and recruitment of individuals with stroke and their families. S/he will be responsible for timely data collection and be knowledgeable in test administration and supported communication strategies for persons with aphasia.

Roberta Virva PT, MS, Site Coordinator (1.2 CAL months for Years 1-5)
Ms. Virva's responsibilities include managing the day to day activities of the project and to oversee and coordinate the activities of the other personnel. She has responsibility for developing systems to monitor progress, to identify problems, and to take appropriate corrective action. She will also participate in analyzing and interpreting results and will participate in the administrative meetings as needed.

TBD, Speech-Language Pathologist (0.24 calendar months for Years 1-4)
The speech-language pathologist (SLP) will report directly to Ms. Virva, the Site Coordinator, to assist with review and coding of SLP therapy activities during data collection. S/he will also advise the research team on questions of eligibility regarding aphasia, and advise the research assistant with regard to interaction with participants and aphasia test administration, as needed.

Salaries are anticipated to increase [redacted] annually

Fringe Rate
Fringe benefits are calculated at [redacted]%

Indirect Costs
The indirect cost rate for subcontracts in this proposal is set at the de minimis rate of [redacted] as MFBRH does not yet have a negotiated F&A rate.

[redacted].

Michigan State University
Dr. Kozlowski is an MSU faculty member with a fixed term employee with contract to MFRH. His effort will be paid through MSU. Subsequently, MSU will receive an Off-campus indirect cost rate[redacted]

Northwestern University

[redacted]
Year 1: 5%
Years 2-5: 15%
[redacted] PhD, will lead this project's Statistical and Data Management Core, which will be responsible for the development and implementation of statistical and data management components of the project, including developing data collection tools and case report forms, setting up the REDCAP database, overseeing data quality throughout the study period, preparing quality assurance reports, and performing statistical analysis of the data. [redacted] has extensive experience as a biostatistician working with observational studies, clinical trials and data management, and she is currently the Leader of the Statistics and Data Management Core leader for a multi-site NIDILRR-funded clinical trial of hypoxia in patients with spinal cord injury.

Data Analyst (MS level)
Year 1: 15%
Years 2-5: 5%
A Data Analyst (MS level) will be hired to work under [redacted] guidance to develop data collection tools and case report forms, set up the REDCap database, produce regular data monitoring reports, and assist with final statistical analyses.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)
Section A, Senior/Key Person	[redacted]
Section B, Other Personnel	[redacted]
Total Number Other Personnel	[redacted]
Total Salary, Wages and Fringe Benefits (A+B)	[redacted]
Section C, Equipment	
Section D, Travel	[redacted]
1. Domestic	[redacted]
2. Foreign	
Section E, Participant/Trainee Support Costs	
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other	
6. Number of Participants/Trainees	
Section F, Other Direct Costs	[redacted]
1. Materials and Supplies	[redacted]
2. Publication Costs	[redacted]
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	[redacted]
6. Equipment or Facility Rental/User Fees	[redacted]
7. Alterations and Renovations	
8. Other 1	[redacted]
9. Other 2	
10. Other 3	
Section G, Direct Costs (A thru F)	[redacted]
Section H, Indirect Costs	[redacted]
Section I, Total Direct and Indirect Costs (G + H)	[redacted]
Section J, Fee	
Section K, Total Costs and Fee (I + J)	[redacted]

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS* [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Northwestern University

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 . [redacted]	[redacted]		[redacted]	PhD	PD/PI	[redacted]	0.60			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Master's Level Statistician	1.80			[redacted]	[redacted]	[redacted]
1	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Northwestern University

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Northwestern University

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period:** 1

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1261-NU Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Northwestern University

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.	[redacted]	[redacted]		[redacted]	PhD	PD/PI	[redacted]	[redacted]			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Master's Level Statistician	0.60			[redacted]	[redacted]	[redacted]
1	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Northwestern University

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS* [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Northwestern University

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1261-NU Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Northwestern University

Start Date*: 04-01-2021 **End Date*:** 03-31-2022 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1.	[redacted]	[redacted]		[redacted]	PhD	PD/PI	[redacted]	0.60			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Master's Level Statistician	0.60			[redacted]	[redacted]	[redacted]
1	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Northwestern University

Start Date*: 04-01-2021 **End Date*:** 03-31-2022 **Budget Period: 3**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Northwestern University

Start Date*: 04-01-2021 **End Date*:** 03-31-2022 **Budget Period:** 3

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1261-NU Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Northwestern University

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period: 4**

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 . Dr.	[redacted]		[redacted]	PhD	PD/PI	[redacted]	0.60			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Master's Level Statistician	0.60			[redacted]	[redacted]	[redacted]
1	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Northwestern University

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period: 4**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Northwestern University

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period:** 4

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1261-NU Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Northwestern University

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 . Dr.	[redacted]		[redacted]	PhD	PD/PI	[redacted]	1.80			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Master's Level Statistician	0.60			[redacted]	[redacted]	[redacted]
1	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Northwestern University

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Northwestern University

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MTDC	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency [redacted]
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1261-NU Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)
Section A, Senior/Key Person	[redacted]
Section B, Other Personnel	[redacted]
Total Number Other Personnel	[redacted]
Total Salary, Wages and Fringe Benefits (A+B)	[redacted]
Section C, Equipment	
Section D, Travel	
1. Domestic	
2. Foreign	
Section E, Participant/Trainee Support Costs	
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other	
6. Number of Participants/Trainees	
Section F, Other Direct Costs	
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Other 1	
9. Other 2	
10. Other 3	
Section G, Direct Costs (A thru F)	[redacted]
Section H, Indirect Costs	[redacted]
Section I, Total Direct and Indirect Costs (G + H)	[redacted]
Section J, Fee	
Section K, Total Costs and Fee (I + J)	[redacted]

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Michigan State University

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 . Dr.	Allan		Kozlowski	PhD	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*

Total Number Other Personnel **Total Other Personnel**

Total Salary, Wages and Fringe Benefits (A+B) [redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Michigan State University

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Michigan State University

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period:** 1

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MODIFIED TOTAL DIRECT COST	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1262-MSU_Budget Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Michigan State University

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 . Dr.	Allan		Kozlowski	PhD	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*

Total Number Other Personnel **Total Other Personnel**

Total Salary, Wages and Fringe Benefits (A+B) [redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Michigan State University

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period:** 2

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Michigan State University

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period:** 2

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MODIFIED TOTAL DIRECT COST	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1262-MSU_Budget Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Michigan State University

Start Date*: 04-01-2020 **End Date*:** 03-31-2022 **Budget Period: 3**

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 . Dr.	Allan		Kozlowski	PhD	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Michigan State University

Start Date*: 04-01-2020 **End Date*:** 03-31-2022 **Budget Period:** 3

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Michigan State University

Start Date*: 04-01-2020 **End Date*:** 03-31-2022 **Budget Period:** 3

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MODIFIED TOTAL DIRECT COST	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1262-MSU_Budget Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Michigan State University

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period: 4**

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 . Dr.	Allan		Kozlowski	PhD	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Total Number Other Personnel					**Total Other Personnel**	
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Michigan State University

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period:** 4

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ● Project ● Subaward/Consortium

Organization: Michigan State University

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period:** 4

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MODIFIED TOTAL DIRECT COST	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1262-MSU_Budget Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Michigan State University

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

A. Senior/Key Person

Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 . Dr.	Allan		Kozlowski	PhD	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*

Total Number Other Personnel **Total Other Personnel**

Total Salary, Wages and Fringe Benefits (A+B) [redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Michigan State University

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period:** 5

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Michigan State University

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period:** 5

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . MODIFIED TOTAL DIRECT COST	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1262-MSU_Budget Justification.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

BUDGET JUSTIFICATION

Subawardee: Michigan State University

SENIOR/KEY PERSONNEL:

Principal Investigator: Dr. Allan Kozlowski will serve as Co-Investigator to provide expertise on longitudinal methodology and statistical modeling on this project. Dr. Kozlowski has the knowledge and experience in study design and model building using hierarchical linear regression methods to capture individual differences in change over time. Funds are requested to support 20% of PI's effort (around 2.4 Person-month) each year over the five years of the project period. An escalation rate of [redacted]% per year for PI's salary has been calculated for the period.

FRINGE BENEFITS:

MSU Faculty and Staff fringes should be calculated using the Specific Identification (SI) method. Under SI, fringe costs are based on average actual costs and individual participation in retirement. MSU charges fringe benefits as direct costs and charges sponsors for actual costs only.

INDIRECT COSTS:

MSU's Facilities and Administrative (F&A) rates is [redacted]% On-campus and [redacted]% Off-campus for the period from July 1, 2016 to June 30, 2019. [redacted]% Off-campus F&A rate is used for this project as Dr. Kozlowski is located in MFB facilities. Modified Total Direct Costs (MTDC) is the base to which the F&A rate is applied. MTDC consists of all direct salaries and wages, applicable fringe benefits, materials and supplies, services, travel and up to the first [redacted] of each subaward. MTDC shall exclude equipment, capital expenditures, charges for patient care, rental costs, tuition remission, scholarships and fellowships, participant support costs and the portion of each subaward in excess of [redacted] This agreement was negotiated through the Department of Health and Human Services, [redacted]

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)
Section A, Senior/Key Person	[redacted]
Section B, Other Personnel	
Total Number Other Personnel	
Total Salary, Wages and Fringe Benefits (A+B)	[redacted]
Section C, Equipment	
Section D, Travel	
1. Domestic	
2. Foreign	
Section E, Participant/Trainee Support Costs	
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other	
6. Number of Participants/Trainees	
Section F, Other Direct Costs	
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Other 1	
9. Other 2	
10. Other 3	
Section G, Direct Costs (A thru F)	[redacted]
Section H, Indirect Costs	[redacted]
Section I, Total Direct and Indirect Costs (G + H)	[redacted]
Section J, Fee	
Section K, Total Costs and Fee (I + J)	[redacted]

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Allan		Kozlowski	PhD	PD/PI	0.00	2.40			[redacted]	[redacted]	[redacted]
2 .	Dr.	John	F.	Butzer	MD	Co-Investigator	0.00	0.60			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Assistant	6.00			[redacted]	[redacted]	[redacted]
1	Site Coordinator	1.20			[redacted]	[redacted]	[redacted]
1	Speech-Language Pathologist	0.24			[redacted]	[redacted]	[redacted]
3	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period: 1**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 1

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2019 **End Date*:** 03-31-2020 **Budget Period:** 1

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Modified Total Direct Costs	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1263-MFB_BudgetJust.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Allan		Kozlowski	PhD	PD/PI	0.00	2.40			[redacted]	[redacted]	[redacted]
2 .	Dr.	John	F.	Butzer	MD	Co-Investigator	0.00	0.60			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Assistant	12.00			[redacted]	[redacted]	[redacted]
1	Site Coordinator	1.20			[redacted]	[redacted]	[redacted]
1	Speech-Language Pathologist	0.24			[redacted]	[redacted]	[redacted]
3	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ❍ Project ● Subaward/Consortium

Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period: 2**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 2

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2020 **End Date*:** 03-31-2021 **Budget Period:** 2

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Modified Total Direct Costs	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1263-MFB_BudgetJust.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2021 **End Date*:** 03-31-2022 **Budget Period: 3**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Allan		Kozlowski	PhD	PD/PI	0.00	2.40			[redacted]	[redacted]	[redacted]
2 .	Dr.	John	F.	Butzer	MD	Co-Investigator	0.00	0.60			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Assistant	12.00			[redacted]	[redacted]	[redacted]
1	Site Coordinator	1.20			[redacted]	[redacted]	[redacted]
1	Speech-Language Pathologist	0.24			[redacted]	[redacted]	[redacted]
3	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2021 **End Date*:** 03-31-2022 **Budget Period:** 3

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 3

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2021 **End Date*:** 03-31-2022 **Budget Period:** 3

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Modified Total Direct Costs	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1263-MFB_BudgetJust.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period: 4**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Allan		Kozlowski	PhD	PD/PI	0.00	2.40			[redacted]	[redacted]	[redacted]
2 .	Dr.	John	F.	Butzer	MD	Co-Investigator	0.00	0.60			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Assistant	6.00			[redacted]	[redacted]	[redacted]
1	Site Coordinator	1.20			[redacted]	[redacted]	[redacted]
1	Speech-Language Pathologist	0.24			[redacted]	[redacted]	[redacted]
3	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period:** 4

C. Equipment Description

List items and dollar amount for each item exceeding $5,000

Equipment Item	Funds Requested ($)*
Total funds requested for all equipment listed in the attached file	
Total Equipment	

Additional Equipment: File Name:

D. Travel	Funds Requested ($)*
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs	Funds Requested ($)*
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other:	
Number of Participants/Trainees — Total Participant Trainee Support Costs	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 4

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2022 **End Date*:** 03-31-2023 **Budget Period:** 4

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Modified Total Direct Costs	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1263-MFB_BudgetJust.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

OMB Number: 4040-0001
Expiration Date: 10/31/2019

RESEARCH & RELATED BUDGET - SECTION A & B, Budget Period 5

ORGANIZATIONAL DUNS* [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Enter name of Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

A. Senior/Key Person

	Prefix	First Name*	Middle Name	Last Name*	Suffix	Project Role*	Base Salary ($)	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits ($)*	Funds Requested ($)*
1 .	Dr.	Allan		Kozlowski	PhD	PD/PI	[redacted]	2.40			[redacted]	[redacted]	[redacted]
2 .	Dr.	John	F.	Butzer	MD	Co-Investigator	[redacted]	0.60			[redacted]	[redacted]	[redacted]

Total Funds Requested for all Senior Key Persons in the attached file

Additional Senior Key Persons: File Name:

Total Senior/Key Person [redacted]

B. Other Personnel

Number of Personnel*	Project Role*	Calendar Months	Academic Months	Summer Months	Requested Salary ($)*	Fringe Benefits*	Funds Requested ($)*
	Post Doctoral Associates						
	Graduate Students						
	Undergraduate Students						
	Secretarial/Clerical						
1	Research Assistant	6.00			[redacted]	[redacted]	[redacted]
1	Site Coordinator	1.20			[redacted]	[redacted]	[redacted]
2	**Total Number Other Personnel**					**Total Other Personnel**	[redacted]
						Total Salary, Wages and Fringe Benefits (A+B)	[redacted]

RESEARCH & RELATED Budget {A-B} (Funds Requested)

Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTION C, D, & E, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period: 5**

C. Equipment Description	
List items and dollar amount for each item exceeding $5,000	
Equipment Item	**Funds Requested ($)***
Total funds requested for all equipment listed in the attached file	
Total Equipment	
Additional Equipment: File Name:	

D. Travel	**Funds Requested ($)***
1. Domestic Travel Costs (Incl. Canada, Mexico, and U.S. Possessions)	
2. Foreign Travel Costs	
Total Travel Cost	

E. Participant/Trainee Support Costs		**Funds Requested ($)***
1. Tuition/Fees/Health Insurance		
2. Stipends		
3. Travel		
4. Subsistence		
5. Other:		
Number of Participants/Trainees	**Total Participant Trainee Support Costs**	

RESEARCH & RELATED Budget {C-E} (Funds Requested)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

RESEARCH & RELATED BUDGET - SECTIONS F-K, Budget Period 5

ORGANIZATIONAL DUNS*: [redacted]

Budget Type*: ○ Project ● Subaward/Consortium

Organization: Mary Free Bed Rehabilitation Hospital

Start Date*: 04-01-2023 **End Date*:** 03-31-2024 **Budget Period:** 5

F. Other Direct Costs	Funds Requested ($)*
Total Other Direct Costs	

G. Direct Costs	Funds Requested ($)*
Total Direct Costs (A thru F)	[redacted]

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)*
1 . Modified Total Direct Costs	[redacted]	[redacted]	[redacted]
		Total Indirect Costs	[redacted]

Cognizant Federal Agency
(Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs	Funds Requested ($)*
Total Direct and Indirect Institutional Costs (G + H)	[redacted]

J. Fee	Funds Requested ($)*

K. Total Costs and Fee	Funds Requested ($)*
	[redacted]

L. Budget Justification*	File Name: 1263-MFB_BudgetJust.pdf (Only attach one file.)

RESEARCH & RELATED Budget {F-K} (Funds Requested)

BUDGET JUSTIFICATION
Mary Free Bed Rehabilitation Hospital
PA17-139
Defining Trajectories of Linguistic, Cognitive-Communicative and Quality of Life Outcomes in Aphasia

Personnel

Allan J. Kozlowski PhD, Site Principle Investigator (2.4 calendar months for Years 1-5)
Dr. Kozlowski is contracted from Michigan State University – College of Human Medicine, Department of Epidemiology and Biostatistics, to be the Director of Outcomes Research at Mary Free Bed Rehabilitation Hospital (MFBRH). As Site PI he will oversee the administration and operations of the Mary Free Bed site and coordinate the communication, interactions and data sharing with the research team at Shirley Ryan AbilityLab. Dr. Kozlowski will play a major role in statistical analysis and data interpretation. He will also participate in administrative meetings. (Dr. Kozlowski's salary is contracted directly from Michigan State University)

John F. Butzer MD, Site Senior Advisor (0.6 calendar months for Years 1-5)
Dr. Butzer is the Director of Research at MFBRH. As a senior manager at MFBRH he will oversee the personnel and address institutional concerns arising from site administration and operations. Dr. Butzer will advise Dr. Kozlowski on institutional and staffing issues. He will also participate in administrative meetings.

TBD, Research Assistant (6 calendar months for Years 1 & 5; 12 calendar months for Years 2-4)
The research assistant will report directly to Ms. Virva, the Site Coordinator, to assist with the engagement and recruitment of individuals with stroke and their families. S/he will be responsible for timely data collection and be knowledgeable in test administration and supported communication strategies for persons with aphasia.

Roberta Virva PT, MS, Site Coordinator (1.2 Calendar months for Years 1-5)
Ms. Virva's responsibilities include managing the day to day activities of the project and to oversee and coordinate the activities of the other personnel. She has responsibility for developing systems to monitor progress, to identify problems, and to take appropriate corrective action. She will also participate in analyzing and interpreting results and will participate in the administrative meetings as needed.

TBD, Speech-Language Pathologist (0.24 calendar months for Years 1-4)
The speech-language pathologist (SLP) will report directly to Ms. Virva, the Site Coordinator, to assist with review and coding of SLP therapy activities during data collection. S/he will also advise the research team on questions of eligibility regarding aphasia, and advise the research assistant with regard to interaction with participants and aphasia test administration, as needed.

Salaries are anticipated to increase [redacted] annually

Fringe Rate
Fringe benefits are calculated at [redacted]

Indirect Costs
The indirect cost rate for subcontracts in this proposal is set at the de minimis rate of [redacted] as MFBRH does not yet have a negotiated F&A rate.

RESEARCH & RELATED BUDGET - Cumulative Budget

	Totals ($)
Section A, Senior/Key Person	[redacted]
Section B, Other Personnel	[redacted]
Total Number Other Personnel	[redacted]
Total Salary, Wages and Fringe Benefits (A+B)	[redacted]
Section C, Equipment	
Section D, Travel	
1. Domestic	
2. Foreign	
Section E, Participant/Trainee Support Costs	
1. Tuition/Fees/Health Insurance	
2. Stipends	
3. Travel	
4. Subsistence	
5. Other	
6. Number of Participants/Trainees	
Section F, Other Direct Costs	
1. Materials and Supplies	
2. Publication Costs	
3. Consultant Services	
4. ADP/Computer Services	
5. Subawards/Consortium/Contractual Costs	
6. Equipment or Facility Rental/User Fees	
7. Alterations and Renovations	
8. Other 1	
9. Other 2	
10. Other 3	
Section G, Direct Costs (A thru F)	[redacted]
Section H, Indirect Costs	[redacted]
Section I, Total Direct and Indirect Costs (G + H)	[redacted]
Section J, Fee	
Section K, Total Costs and Fee (I + J)	[redacted]

Total Direct Costs less Consortium F&A

NIH policy (NOT-OD-05-004) allows applicants to exclude consortium/contractual F&A costs when determining if an application falls at or beneath any applicable direct cost limit. When a direct cost limit is specified in an FOA, the following table can be used to determine if your application falls within that limit.

Category	Budget Period 1	Budget Period 2	Budget Period 3	Budget Period 4	Budget Period 5	TOTALS
Total Direct Costs less Consortium F&A	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]

PHS 398 Cover Page Supplement

OMB Number: 0925-0001

Expiration Date: 03/31/2020

1. Vertebrate Animals Section

Are vertebrate animals euthanized? ○ Yes ● No

If "Yes" to euthanasia

Is the method consistent with American Veterinary Medical Association (AVMA) guidelines?

○ Yes ○ No

If "No" to AVMA guidelines, describe method and provide scientific justification

2. *Program Income Section

*Is program income anticipated during the periods for which the grant support is requested?

○ Yes ● No

If you checked "yes" above (indicating that program income is anticipated), then use the format below to reflect the amount and source(s). Otherwise, leave this section blank.

*Budget Period	*Anticipated Amount ($)	*Source(s)

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

PHS 398 Cover Page Supplement

3. Human Embryonic Stem Cells Section

*Does the proposed project involve human embryonic stem cells? ○ Yes ● No

If the proposed project involves human embryonic stem cells, list below the registration number of the specific cell line(s) from the following list: http://grants.nih.gov/stem_cells/registry/current.htm. Or, if a specific stem cell line cannot be referenced at this time, check the box indicating that one from the registry will be used:

Specific stem cell line cannot be referenced at this time. One from the registry will be used.

Cell Line(s) (Example: 0004):

4. Inventions and Patents Section (Renewal applications)

*Inventions and Patents: ○ Yes ○ No

If the answer is "Yes" then please answer the following:

*Previously Reported: ○ Yes ○ No

5. Change of Investigator/Change of Institution Section

❑ Change of Project Director/Principal Investigator

Name of former Project Director/Principal Investigator

Prefix:

*First Name:

Middle Name:

*Last Name:

Suffix:

❑ Change of Grantee Institution

*Name of former institution:

Tracking Number: GRANT12670047 Funding Opportunity Number: PA-18-287 . Received Date: 2018-07-05T15:37:27.000-04:00

PHS 398 Research Plan

OMB Number: 0925-0001
Expiration Date: 03/31/2020

Introduction	
1. Introduction to Application (for Resubmission and Revision applications)	1247-Heinemann_Intro.pdf
Research Plan Section	
2. Specific Aims	1248-Heinemann_SpecAims.pdf
3. Research Strategy*	1249-Heinemann_ResStrat.pdf
4. Progress Report Publication List	
Other Research Plan Section	
5. Vertebrate Animals	
6. Select Agent Research	
7. Multiple PD/PI Leadership Plan	1250-HeinemannCherney_MultPI.pdf
8. Consortium/Contractual Arrangements	1251-Heinemann_LOI.pdf
9. Letters of Support	1252-Heinemann_LOS .pdf
10. Resource Sharing Plan(s)	1253-Heinemann_DataSharPlan.pdf
11. Authentication of Key Biological and/or Chemical Resources	
Appendix	
12. Appendix	

Tracking Number: GRANT12670047
Funding Opportunity Number: PA-18-287. Received Date: 2018-07-05T15:37:27.000-04:00

Introduction to the Revised Submission

The reviewers identified several concerns, including absence of a theoretical model and mechanistic hypotheses, generalizability of study findings, limited aphasia expertise, additional variables that could influence aphasia recovery, inclusion criteria, and fMRI procedures. This revised submission addresses these concerns.

Absence of a Theoretical Model and Mechanistic Hypotheses: A reviewer noted that the application did not specify clearly the mechanisms by which predictors might interact to influence the course of aphasia recovery and observed that the development of a holistic path model for aphasia recovery would be of great significance. The reviewer noted that we specified factors that may be important for cognitive, linguistic, and QOL outcomes, but noted the absence of socioeconomic status, history of psychiatric disorder, major medical comorbidities, leukoaraiosis, and prescribed medications, particularly SSRIs. In this revision, we provide a model (Figure 2) that describes hypothesized relationships between model components (e.g., genomic testing with treatment dosage). We appreciate and adopted the suggestion to include additional factors that may contribute to cognitive, linguistic, and QOL outcomes, and included them in this revision.

Relatedly, a reviewer noted the absence of hypotheses to guide analyses involving genetic tests and justification of specific genes. This revision clarifies that we selected SNPs based on published studies, including Brain Derived Neurotrophic Factor, Apolipoprotein E, Insulin Growth Factor 1, Catechol-O-methyltransferase, Fibroblast Growth Factor 2, and Vascular Endothelial Growth Factor A. We provide citations justifying the SNPs based on demonstrated modulation of neuroplasticity in stroke patients and effects on stroke recovery.

Generalizability of Study Findings: A reviewer noted that all sites are in the Midwestern U.S. and was concerned that results may not generalize. While all study sites are within 200 miles of each other, we revised the facility descriptions to emphasize the diverse demographic and stroke characteristics. We will treat “facility” as a fixed effect and examine site as a factor. We report information about the representativeness of stroke patients served by the collaborating inpatient rehabilitation facilities (IRFs) in Human Subjects, and demonstrate that we will recruit a demographically-representative sample with a wide range of stroke severity.

Clinical and Research Expertise in Stroke and Aphasia: A reviewer was concerned that team members do not have aphasia research experience. While not all team members have extensive aphasia experience, co-PI Cherney is an international expert on aphasia recovery and treatment; co-PI Heinemann is a coauthor on several of her publications.[1,2] Other key personnel bring expertise in individual growth curve modeling with rehabilitation populations (Kozlowski[3-8]), advanced biostatistical design (Kocherginsky), and quality of life research (Heinemann[9,10]). We share authorship on several stroke-related manuscripts. Cherney and Baliki have worked together over the last 18 months and have conducted two aphasia studies using fMRI. One has been accepted for publication in *Neurorehabilitation*.[11] We have revised the key personnel’s personal statements to highlight their aphasia and collaborative experience, as well as their unique contribution to this project. Research assistants with direct contact with participants will receive extensive training about aphasia, supported communication, and test administration for persons with aphasia from co-PI Cherney and research speech-language pathologist (SLP) Hurwitz, who has over 10 years of experience evaluating persons with aphasia.

Additional Variables Affecting Retention and Aphasia Recovery: A reviewer noted factors that could influence aphasia recovery and attrition, including neurologic conditions, global health status, and medical conditions that could affect recovery such as congestive heart failure, advanced stage cancer, and end stage renal disease. In response, we will assess these factors and have added plans to evaluate nonrandom attrition and aphasia recovery. A reviewer suggested that we consider adding an MRI sequence to quantify leukoaraiosis. We appreciate this insight and now propose the required sequences and analytic tools.

Inclusion Criteria: A reviewer was concerned that requiring participants to provide informed consent would exclude individuals with significant comprehension deficits and reduce generalizability of the results. We acknowledge that attrition may vary by extent of recovery, SES, health status, and other non-random factors. We will train staff members who are consenting patients to use supported communication strategies with picture-based materials. This protocol will allow us to consent a large proportion of patients with severe aphasia.

Need for Careful Registration Procedures in fMRI: A reviewer was concerned regarding normalization of stroke brains to standard templates and lack of details regarding rs-fMRI analyses. We now describe registration procedures in greater detail, including linear and non-linear registration that decrease warping in brains with large strokes. In addition to utilizing the Human Connectome Project pipelines, we will use specific registration tools that are optimized for stroke. We clarify that only patients at SRALab will be scanned using the 3T Siemens Prisma. We will use different atlases and parcellation schema in our resting state and anatomical analyses. Brain networks will be constructed using either a whole brain voxel-wise approach or various validated parcellation schemas ranging from 90 - 500 ROIs. We will include white matter and subcortical regions.

Specific Aims

Stroke is a major public health issue with life-long consequences for millions of survivors and their caregivers. Aphasia is a common consequence with a prevalence of approximately 2,000,000.[12] Rehabilitation approaches for aphasia continue to evolve, though we know little about the dose, timing, and components of therapy that could ameliorate cognitive, linguistic, and communicative deficits. Needed is an adequately powered, prospective study of a cohort in which we can evaluate models of aphasia recovery considering person, stroke, and therapy characteristics. This longitudinal cohort study evaluates a multi-faceted model of linguistic, cognitive-communicative, and health-related quality of life (QoL) recovery in persons with stroke-related aphasia up to 18 months after onset, and evaluates the contribution of patient, stroke-related, and treatment factors that affect outcomes. Language recovery in post-stroke aphasia is variable and difficult to predict.[13-18] A multitude of factors including demographic, clinical, and treatment variables affect short- and long-term outcomes. However, there is limited agreement on the extent to which these factors predict recovery. Results across studies may be contradictory because of methodological differences including the heterogeneity of samples, the selection of outcome measures with most studies using only linguistic measures, small samples, and retrospective designs. To understand aphasia recovery better, there is a critical need for a large, prospective, methodologically-sound study that takes into consideration these issues.

Some factors such as therapy utilization can be modified to improve outcomes. Our earlier work[19-21] described therapy utilization during stroke rehabilitation and evaluated the contribution of therapy characteristics and length of stay to functional gains. Therapy intensity accounted for about ¼ of the variance in functional gains. This work was a valuable first step in describing therapy utilization and sets the stage for a focused study of speech and language therapy utilization for persons with aphasia, a description of functional gains during rehabilitation, and tracking of patients after discharge. Frequent assessments will allow us to describe the course or *trajectory* of recovery. Defining recovery trajectories will allow clinicians to know when patients are recovering on par with, exceeding, or lagging behind expected recovery, and to modify therapies to optimize function and QoL.

In addition to therapy characteristics which may affect language recovery, patient factors including demographic and clinical characteristics such as the type and severity of the initial aphasia, the size and location of the lesion, and variability in brain networks may affect recovery.[17,22] Variations in genetic polymorphisms such as brain-derived neurotrophic factor (BDNF) affect neuroplasticity and may affect response to rehabilitation.[23-25] We include these factors in a model of aphasia recovery which we will test empirically. Patients' perspectives on their linguistic and communicative outcomes and QoL are also critical in monitoring and improving rehabilitation services; however, rehabilitation programs rarely collect patient-reported outcome measures (PROMs).

We propose a model of aphasia recovery that identifies both patient factors and treatment variables as key predictors of aphasia recovery. Our overall goal is to evaluate a model using individual growth curve analysis as a method to understand better the linguistic, cognitive-communicative, and health-related QoL outcomes in adults with post-stroke aphasia. We will investigate the association of patient factors (i.e., demographic and clinical characteristics) and treatment variables on outcomes. We will also determine the effects of neurobiological patient factors such as brain and genetic biomarkers in this model of aphasia recovery. We will recruit a large cohort of patients with aphasia from three IRFs and follow them through inpatient and outpatient therapy to 18 months. The Specific Aims are to:

Aim 1: Establish a prospective cohort of stroke patients with aphasia, and define their typical trajectory of linguistic, cognitive-communicative, and health-related QoL recovery at admission to and discharge from the IRF, and at 6, 12, and 18 months post onset.

Aim 2: Identify factors within the proposed model that are associated with linguistic, cognitive-communicative, and health-related QoL outcomes from among:

- **a)** Patient factors, including demographic and clinical characteristics related to stroke and aphasia;
- **b)** Treatment variables, including inpatient and outpatient aphasia therapy characteristics and informal aphasia services; and
- **c)** Biomarkers, including genetic and neuroimaging biomarkers.

Aim 3: Evaluate the stability of the models of linguistic, cognitive-communicative, and health-related QoL outcomes recovery that are developed in Aim 2.

We expect that findings from this large, prospective longitudinal cohort study will provide a detailed understanding of the effects of speech and language therapy characteristics and other participant and aphasia-related factors on patients' outcome trajectories, which will inform clinical practice and rehabilitation service delivery during and following inpatient rehabilitation.

Significance

Stroke and Aphasia Epidemiology: Approximately 17 million people worldwide experience a first stroke annually[26] of which 610,000 occur in the United States.[27] Although stroke prevalence has remained relatively stable,[28,29] stroke prevalence will likely rise due to the aging population and increasing rates of stroke risk factors, including diabetes mellitus, obesity, and physical inactivity.[27] Advances in acute stroke treatment and inpatient management have improved stroke survival greatly[30] with fewer than 130,000 deaths occurring per year,[28,31] and a 38% decrease in stroke-related mortality from 2000 to 2010.[28,29,32] However, stroke remains a leading cause of long-term disability.[27] One of the most devastating consequences of stroke is aphasia, which occurs in about 1/3 of patients.[33-35] Aphasia impairs, to varying degrees, understanding and expression of oral language, reading, and writing. Reduced language skills can have significant negative effects on participation in rehabilitation and subsequent functional outcomes, as well as on social, vocational, and recreational activities. People with aphasia report isolation, loneliness, loss of autonomy, restricted activities, role changes, stigmatization and depression.[36-41] Aphasia is not just an acute event, but has continuing effects.[42,43] Aphasia affects family and friends, with a growing literature recognizing the negative effects on family and community life.[44-50] As more individuals survive acute stroke, the need for effective rehabilitation strategies to reduce aphasia-related disability becomes urgent.

Limitations of Current Treatment Services: Approaches to the management and rehabilitation of aphasia continue to evolve. The medical model focuses on treating impairment and restoring language function.[51] Over the past two decades, therapists have embraced functional/social models of intervention that focus on the broad life context of the person.[52-54] Despite research on the importance of participation for persons with aphasia, health care policies and insurance coverage of treatment have not kept up with this paradigm shift. Insurers typically cover therapy that targets impairments, and evidence supporting an association between impairment-based treatment and broader outcomes related to communication and QoL is lacking.

The duration and intensity of rehabilitation therapy is severely limited.[55-58] The timing, amount, and duration of inpatient therapies and the facility where patients receive rehabilitation services depends greatly on insurance coverage. Commercial insurers usually adopt the Centers for Medicare and Medicaid Services (CMS) therapy requirements; however, there is great variability in the extent of coverage due to varying definitions of medical necessity. CMS requires IRFs to deliver 3 hours of therapy per day at least 5 days per week, although there is limited evidence to support this level of therapy intensity. Patients may receive 3 hours per day through a combination of physical therapy (PT), occupational therapy (OT), and speech-language pathology (SLP) services. Persons with aphasia may receive limited treatment targeting their language and communication deficits during an IRF stay. The mean length of stay in an IRF for stroke rehabilitation is 14.6 days.[59] For outpatient rehabilitation, CMS imposes therapy caps that limit rehabilitation services based on expenditures. The 2018 therapy caps are [redacted] for PT and SLP therapy services combined, and [redacted] for OT services. In practice, most patients reach these therapy caps in less than two months. Thus, patients who receive both inpatient and outpatient rehabilitation exhaust their benefits within three months. Insurers limit rehabilitation despite the accumulating evidence on neural plasticity that indicates the importance of intensive therapy in rehabilitation[60-63] as well as studies demonstrating that even those with chronic aphasia may benefit from intensive treatment.[64-66]

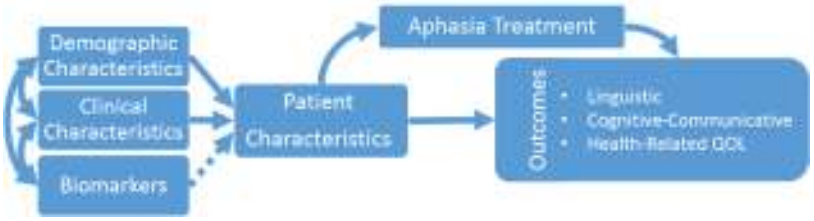
Understanding the trajectories of functional recovery and QoL improvement – and how this is related to therapy exposure – will enable post-acute care providers to develop an evidence base that enables clinicians to plan rehabilitation therapies that are tailored to individual needs, and maximize functional and QoL outcomes while minimizing the cost of stroke rehabilitation.

Quality of Life after Stroke: Stroke survivors experience reduced QoL compared to age-matched peers;[67,68] they often face limitations in performing housework, shopping, preparing meals, and traveling beyond their community. Functional limitations result in social isolation, depression, and a lack of purpose.[67,68] Aphasia reduces QoL further.[41,69] People with aphasia report worse QoL after stroke than people without aphasia, even when their physical abilities, well-being, and social support are comparable.[41,70] Although disability is prevalent, most patients achieve functional gains during IRF stays. Patients who receive inpatient stroke rehabilitation achieve a mean gain of 29.7 points on total Functional Independence Measure (FIM™) scores (108 point range); their mean gain on Motor FIM™ scores is 24.2 points (78 point range), and Cognitive FIM™ scores gain 5.5 points (30 point range).[71] Reducing functional limitations, including communication through effective rehabilitation therapies may result in improved overall QoL.

The Trajectory of Aphasia Recovery: Language recovery in post-stroke aphasia is variable and difficult to predict even in the first 90 days post-stroke.[13-18] A multitude of interacting variables affect short- and long-term outcomes. Figure 2 illustrates the interaction of these variables and their effects on outcomes. We distinguish three categories of outcomes: linguistic, cognitive-communicative, and health-related QOL. We suggest that the major

contributors to achievement of these outcomes are patient characteristics and the aphasia treatment that they receive. We know little about patterns of recovery for linguistic, cognitive-communicative, and QOL outcomes after stroke. Effective aphasia treatment requires that we understand factors associated with higher plateaus of recovery, faster recovery rates, and both higher plateaus and faster recovery rates.

Figure 2. Model of Linguistic, Cognitive-Communicative, and Health-Related QoL Outcomes



Patient characteristics include demographic characteristics such as age, sex, education, SES, and handedness, as well as clinical variables that are related to the stroke such as lesion size and location, stroke severity, type and severity of aphasia, medical comorbidities, and medications. Genetic and brain biomarkers may influence the expression of patient characteristics. While patient characteristics typically cannot be modified to any great extent, aphasia treatment variables, including type, amount and intensity, can be modified in order to maximize outcomes.

There is limited agreement on the extent to which specific variables predict recovery. For example, lesion size is an important predictor of recovery in most[72,73] but not all studies,[16,73] with larger lesions predicting poorer aphasia recovery. Yet a lesion occurring in a critical language area may be a more important predictor of language recovery than lesion size alone.[74,75] New methods suggest that the integrity of areas remote from the lesion and alterations in network connectivity affect language recovery.[76-79] Patient factors such as sex, age, handedness, and education have been the focus of investigation, often with inconclusive results.[15,17,22] Similarly, the type and initial severity of aphasia affect recovery in some, but not all, studies.[75,80,81] Results may appear contradictory because of methodological differences including the heterogeneity of samples, the selection of outcome measures, with most studies only selecting linguistic measures, such as the Western Aphasia Battery-Revised (WAB-R),[82] and the timing of end-point assessments. Many studies recruited small sample sizes, and not all the studies are prospective. To understand aphasia recovery better, there is a critical need for large, prospective, methodologically sound studies that take into consideration multiple factors that affect outcomes.

With regard to aphasia treatment, hundreds of studies, systematic reviews, meta-analyses and expert opinion conclude that aphasia treatment is beneficial.[83-86] Although there is little evidence indicating that one treatment is more effective than others,[86 13] there is an accumulating body of evidence that suggests the amount, intensity, and duration of therapy affects recovery regardless of the type and severity of the aphasia.[75,86-89] Yet, we know little about the characteristics of aphasia therapy provided during inpatient rehabilitation, the gains made during this early treatment period, and long-term outcomes. Given the chronicity of the disorder, individuals typically seek continuing outpatient treatment in hospital and university clinics, as well as alternate services through aphasia centers,[90,91] intensive comprehensive aphasia programs,[92,93] and research studies. Any model of aphasia recovery must consider variables associated with treatment both during and after inpatient rehabilitation.

Genetic Variations May Affect Outcomes: Genetic variations are genome-wide modifications in DNA sequences among individuals of a population. Unlike genetic mutations, polymorphisms are relatively frequent DNA variations that are not disease-causing but can affect physiological systems, especially when interacting with other genetic variants or environmental cues.[94] Single-nucleotide polymorphisms (SNP) are a common type of polymorphism; they are a variation of the genetic code in a single base pair wherein one nucleotide replaces another, leading to changes in gene or protein sequence, expression, structure, and activity. SNPs can lead to biological variations in molecular and cellular processes that have functional and systemic consequences.[94,95]

Stroke activates multiple biological pathways, neuroprotective or detrimental to the brain, resulting in neurophysiologic, hemodynamic, and biochemical changes that determine outcome. Increasingly, patient management includes an evaluation of disease-related genetic polymorphisms affecting neuroplasticity, which is the ability of neural networks to adapt their functional organization at the cellular and molecular levels in response to stroke and post-stroke rehabilitation.[23,96] Language recovery may be mediated by neuroplasticity.[97 98] One contributor to language recovery could be genetic predisposition based on neuroplasticity-associated SNPs.

Despite promising advances in identifying SNPs associated with post-stroke motor and cognitive skill recovery,[24,99,100] identification of SNPs predictive of language recovery in stroke patients has been relatively unsuccessful. A recent study investigating the influence of the BDNF Val66Met polymorphism on language recovery in post-stroke aphasia found no significant differences between carriers and noncarriers in the level of language improvement, suggesting that the BDNF polymorphism alone did not influence aphasia recovery.[101] Another study suggested a nearly statistically significant increase in prevalence of aphasia in stroke patients with the

genotype APOE-ε4 compared with other APOE genotypes.[102] Many complex human diseases and traits cluster in families and are influenced by interaction of multiple genetic and environmental factors.[103] Therefore, we will consider the interactions (epistasis) between multiple neurotrophic factors and their polymorphisms rather than individual SNPs. We will investigate the genetic association and interactions of SNPs in genes that are linked to neuroplasticity at the cellular and molecular level in post-stroke recovery,[104] including growth factors mediating neurogenesis, angiogenesis, synaptic remodeling, and neuroprotection (see Table 4 for specific polymorphisms and references). We will use multifactor dimensionality reduction statistical methods[10] to identify significant genetic outcome predictor models. We hypothesize that language recovery after stroke is modulated by epistatic interactions between two or more SNPs. We will integrate this genetic analysis with other factors (neuroimaging, clinical and demographic characteristics) as part of a model that provides a detailed understanding of the effects of speech and language therapy and other aphasia-related factors on patients' outcome trajectories.

Baseline Network Status May Be a Biomarker of Recovery: A resting state, functional magnetic resonance imaging (rs-fMRI) scan captures brains activity when a participant is not performing a specific task. A recent stroke recovery and rehabilitation consensus statement identified resting state functional connectivity as a promising candidate biomarker of recovery.[105] Several studies suggest that measures of inter- and intra-network connectivity predict outcomes and treatment response across multiple domains. Only a few studies have explored rs-fMRI in aphasia[76-78,106] with results indicating a relationship between aphasia severity and an acute disruption of connectivity within the language network.[107] However, small samples and different analytical approaches limit interpretation. We will use multi-modal brain imaging techniques such as diffusion tensor imaging and rs-fMRI in a subsample of 100 participants. The ease with which these brain images are acquired make it a practical method for persons with limited ability to perform tasks during an fMRI because of aphasia.[76] More importantly, an increasing body of evidence from clinical studies show that baseline brain properties play a key role in the emergence and manifestation of behavioral symptoms in multiple neurological disorders.[108] rs-fMRI has been used to identify the neural networks underlying language processing and their modulation in response to therapy.[107] While changes in interhemispheric connectivity appear to be consistently related to language deficits, functional correlates underlying aphasia and its recovery remains relatively unexplored due to small populations and the lack of structured longitudinal studies that examine short and long term outcomes.[107] Within this framework, the study proposed here will be seminal in identifying the brain mechanisms that influence aphasia recovery.

Advances in Modeling Outcomes: Rehabilitation outcomes, unlike those in other areas of medicine, evolve over prolonged periods, and commonly result in permanent residual impairments, activity limitations, and participation restrictions. Consequently, outcomes of recovery after stroke are not suited to point-in-time difference measurements (e.g., admission to discharge), which complicates efforts to evaluate the effectiveness of therapies provided to augment recovery. Service-based outcome measurement procedures, such as those required for IRFs, measure at admission and discharge on a trajectory that continues to improve. Even when measurements are made at multiple times, group-level analyses preclude interpretation of individual differences in recovery patterns,[109,110] limiting their utility and translation to clinical practice.

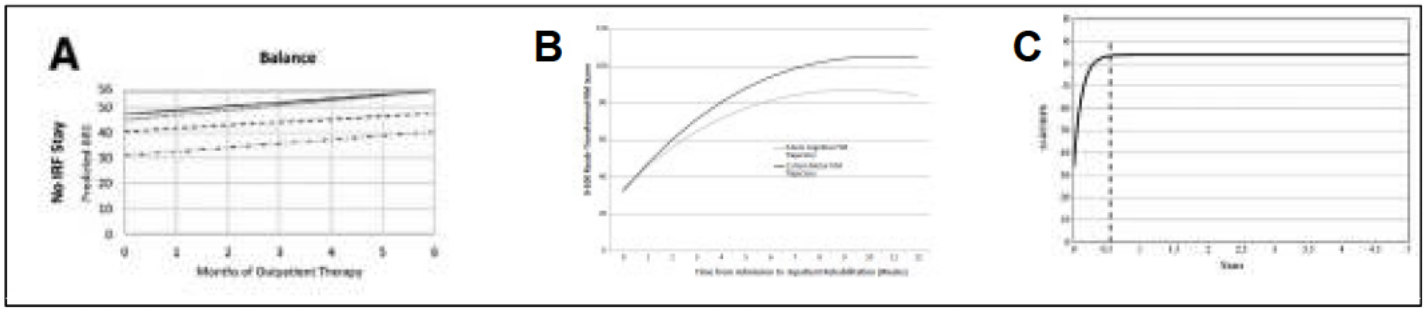


Figure 1: Longitudinal Models. Outcomes modeled longitudinally can be fit with different mathematical functions depending on how individual-level data are distributed over time. **(A)** Lohse et al. modeled recovery of balance and timed walk data from outpatients as linear trajectories, defined by an intercept and constant rate of change.[111] **(B)** Hart et al. modeled motor and cognitive recovery after traumatic brain injury during inpatient rehabilitation as curvilinear (cubic) trajectories, defined by an intercept and instantaneous rate of change.[4] **(C)** Pretz et al. modeled motor recovery after spinal cord injury from inpatient rehabilitation through community life as non-linear (negative exponential) trajectories), defined by three parameters that describe rapid change to a plateau.[5] Personal, condition, treatment, and/or social/environmental can explain individual-level variance in the trajectories providing descriptions of the path of recovery at the individual-level, which could potentially serve as patient-specific prognoses.

Longitudinal designs that employ mixed-effects methods allow us to describe individuals' change over time.[109,110,112,113] These methods include individual growth curve (IGC) models, also known as random slopes and intercepts models, which have been used to describe recovery for persons with spinal cord injury,[3,5,6,114] acquired brain injury,[4,115-117] and stroke.[7,118] Trend lines, or trajectories, are modeled simultaneously for each person, where the trajectory shape is determined by the best fit to the data (Figure 1). Instead of modeling and

comparing group differences as means at each time point, the group trend (fixed effects) is modeled as the average of the intercept and slope for the individual trend lines. Individual differences in the trajectory parameters (random effects) are also modeled; thus, we can test between-group differences and covariate associations with trajectory parameters. Differences on the intercept indicate individual variability at baseline, and differences on the slope indicate individual variability in rates of change. We can model various trajectories including linear (Figure 1A), curvilinear (1B), and non-linear trajectories (1C), depending on which function best fits the data.

These models retain individual differences and describe outcomes as trajectories for individuals defined by a set of covariate associations, such as demographic, impairment, and therapy characteristics: they can explain individual variations on trajectory parameters. For example, we developed an IGC model using FIM™ motor scores for persons with paraplegia.[5] The majority of functional recovery occurs during the first year post-injury, but Pretz[5] demonstrated that individuals also vary in the time from admission to when gains diminish.[5] Knowledge of the expected level and timing of a plateau for a given individual allows therapists to sequence and time therapies to patients' unique needs. IGC models also allow construction of individual-level trajectories based on specific values of the covariates in the model[112] enhancing personalized rehabilitation. Longitudinal models represent the most appropriate method to describe recovery and to examine between-group and individual differences related to rehabilitation therapies received during and following inpatient rehabilitation.

Innovation

Understanding recovery trajectories at the individual level is a crucial first step toward extending the promise of precision medicine to rehabilitation. Our objective is to describe and predict the trajectories of recovery over the first 18 months following stroke, using standardized assessments to evaluate linguistic, cognitive-communicative, and QoL changes. The aims of this proposal are innovative and timely. There are no prospective, longitudinal, multi-site studies that report trajectories of aphasia recovery to 18 months *and* their associations with patient, lesion, aphasia, genomic, and rehabilitation characteristics. This study is innovative in seven respects: (1) We will use standardized assessments that extend beyond linguistic assessments such as the WAB-R to include communication and QoL measures; QoL measures have seldom been included as outcome measures in aphasia studies.[119] (2) We will use patient-centered, self-report instruments including Neuro-QoL which was developed with modern, mixed methods that included patient and clinician input. The Neuro-QoL measurement system assesses concerns that are relevant to patients, but research with this instrument has typically excluded patients with aphasia; its use here allows us to compare our sample with population norms. (3) We will use novel IGC models to describe recovery trajectories and examine associations between demographic, lesion, aphasia, genetic, and speech and language therapy characteristics. IGC modeling allows us to build interactive tools to describe individual trajectories, which will provide clinicians with evidence-based prognoses. Trajectories generated by an interactive tool based on multiple characteristics represent a patient-centered approach, which will provide the best-available evidence for recovery potential of new patients. (4) To identify new genetic pathways involved in language recovery following stroke, we will assess the association between multiple SNPs and biomarkers that may promote neuroplasticity and assess their association with recovery from aphasia up to 18 months post-stroke. (5) We will use a novel technology (rs-fMRI) to explore the functional connectivity in resting state networks in 100 participants and evaluate the association of network pathology with recovery from aphasia at 18 months post-stroke; doing so allows us to identify specific and objective biomarkers and explore the brain mechanisms underlying aphasia recovery. (6) We will collect information on the type, amount, and duration of aphasia treatment provided at three IRFs and assess the association of inpatient therapy with outcomes at 18 months. Although there is a large research literature on the efficacy of aphasia treatment when provided in controlled, experimental environments, few investigations have focused on aphasia treatment in clinical settings. (7) We will collect data related to services and other activities that persons with aphasia participate in following discharge from formal therapy, allowing us to test an integrative model of aphasia recovery.

Cumulatively, this study will provide comprehensive resources for clinicians in modeling aphasia recovery and support the development of patient-centered therapies. A better understanding of recovery can assist with prognosis, allowing patients and caregivers to plan, helping clinicians choose appropriate therapies, providing benchmarks against which to measure change, and allowing therapy adjustments if patients do not attain benchmarks.

Responsiveness to PA-17-139: This application addresses a primary topic listed in the funding announcement, specifically *identifying patient and provider variables that predict outcomes for adults with communication disorders*, including QoL and psychosocial adjustment. Investigators have expertise in health services and outcomes research, adult neurological communication disorders with a specific focus on aphasia treatment research, growth modeling and statistics, genomics, and imaging. The project focuses on practice-relevant questions and follows individuals with aphasia in diverse, real-world settings.

Approach

Overview

We propose an observational cohort study at three IRFs with expertise in stroke-related aphasia. We will assess function weekly during the IRF stay with the IRF Patient Assessment Instrument; at admission and discharge with the NIH Stroke Scale; and at admission and/or discharge, 6-, 12-, and 18-months post-stroke with selected linguistic assessments and self-report instruments as outlined in Table 3. We will extract information about speech and language therapy from in- and outpatient records. Speech therapists at each site will document therapy sessions on a template that allows abstraction of therapy details. We will use IGC models for analysis of recovery trajectories.

Study Population: We will enroll individuals admitted to each of three Joint Commission-accredited IRFs: The Shirley Ryan AbilityLab, Alexian Brothers Rehabilitation Hospital in Elk Grove Village, IL, and Mary Free Bed Rehabilitation Hospital in Grand Rapids, MI, for a total of 300 patients followed to 18 months. Inclusion criteria are a primary diagnosis of a first stroke with aphasia, age 21 years and older, and first admission for inpatient rehabilitation. Table 2 shows the number of stroke admissions with aphasia over the past fiscal year. Based on our experience with a Patient-Centered Outcomes Research Institute-funded study requiring patient self-report capacity,[10] as well as the percentage of patients who are likely to consent to participate, we expect to complete enrollment within 30 months. As described in the power analysis, a sample of 300 at 18 months allows a robust longitudinal analysis and provides sufficient power to estimate the IGC models. We will over-recruit by 100 patients (400 consented patients), estimating 15% attrition by 6-months and another 10% attrition by 18-months.

Table 2. Stroke Patient Admissions with Aphasia at Participating IRFs and Likely Sample in Past 12 Months

Inpatient ‘Rehabilitation Facility	Admissions	Eligible	Likely to Consent
Shirley Ryan AbilityLab (AbilityLab)	[redacted]	[redacted]	[redacted]
Alexian Brothers Rehabilitation Hospital (ABRH)	[redacted]	[redacted]	[redacted]
Mary Free Bed Rehabilitation Hospital (MFBRH)	[redacted]	[redacted]	[redacted]
Totals	[redacted]	[redacted]	[redacted]

Aims and Hypotheses

Aim 1: Establish a prospective cohort of stroke patients with aphasia, and define their typical patterns (trajectories) of linguistic, cognitive-communicative, and health-related QoL recovery.

Hypothesis 1: Linguistic outcomes (WAB-R AQ) improve to 6-months post-stroke and then slow, whereas cognitive-communicative outcomes (CPIB) and QoL outcomes improve to 18-months post-stroke.

Aim 2: Identify factors that are associated with linguistic, cognitive-communicative, and health-related QoL outcomes from among:

- **a)** Patient factors, including demographic and clinical characteristics related to stroke and aphasia;
- **b)** Treatment variables, including inpatient and outpatient aphasia therapy characteristics and informal aphasia services; and
- **c)** Biomarkers, including genetic and neuroimaging biomarkers.

Hypothesis 2a: Patients with smaller lesions, fewer comorbidities, and less severe initial aphasia achieve greater gains in linguistic, cognitive-communicative, and health-related QoL than patients with larger lesions, more comorbidities, and more severe aphasia.

Hypotheses 2b: Patients who begin speech and language therapy earlier and receive therapy that is more intensive and longer in duration achieve greater linguistic, cognitive-communicative, and health-related QoL than patients who begin speech and language therapy later and receive less intensive therapy. And,

Patients who receive longer duration outpatient and other formal and informal aphasia services achieve greater linguistic, cognitive-communicative, and health-related QoL than patients who receive shorter periods of therapy.

Hypothesis 2c: Biomarkers including the presence or absence of critical neuroplastic polymorphisms and the degree of resting state connectivity interact with patients’ demographic and clinical characteristics to influence linguistic, cognitive-communicative, and health-related QoL outcomes.

Aim 3: Evaluate the stability of the linguistic, cognitive-communicative, and health-related QoL outcomes recovery models from Aim 2.

Hypothesis 3: Models selected in Aim 2 will be stable, that is, the variables in the final model appear in the majority of bootstrapped replications, and prediction error (i.e., the difference between an observed and predicted score at any time point) is no greater than the minimally clinical important difference for each outcome.

Preliminary Studies

Characterization of Therapy Components: We described patterns of therapy utilization during inpatient rehabilitation and evaluated the importance of rehabilitation service characteristics in terms of focus, intensity, and length of stay on functional gains.[19-21] Controlling for stroke severity, longer lengths of stay and more intensive function-focused OT predicted self-care gains, while longer stays predicted cognitive gains. In this earlier work, persons with aphasia were not represented adequately, a common occurrence in stroke research. We also assessed patient status at IRF admission and discharge only, leaving us unable to describe the trajectory of patient improvement and how a mix of therapies contributed to longer-term functional gains. To plan clinical interventions, clinicians need detailed information about the trajectory of change that patients are likely to experience during and following inpatient stroke rehabilitation and how rehabilitation therapies affect recovery trajectories.

Individual Growth Modeling of Recovery Trajectory: We developed an IGC model using FIM™ motor subscale data for persons with paraplegia in the SCI Model Systems National Database.[5] Most recovery from SCI occurs during the first year post-injury, but we demonstrated that recovery of individuals with specific demographic, injury, and rehabilitation characteristics can slow at different times after rehabilitation admission.[5] We also constructed an individual-level trajectory model based on specific values for the covariates included in a model; clinicians can use this model to facilitate treatment planning.[5,112]

Extraction and Analysis of Therapy Data from Billing Records: We extracted therapy charges for 71 stroke patients admitted in a recent month from AbilityLab billing records. Patients had a median length of stay of 12 days (SD=9.2). The median quarter-hour units of PT, OT, and SLP was [redacted] and the median daily number of quarter-hour units was [redacted] While the daily median PT and OT units were correlated strongly (0.61), the relationship between PT and SLP and OT and SLP was weaker [redacted] Length of stay was negatively correlated with each discipline's therapy units [redacted] such that patients with longer stays tended to receive fewer services per day. OT, PT, and SLP units were correlated negatively [redacted] with length of stay. However, billing records do not contain the information about therapy activities that IRF SLPs will log during their treatment sessions.

Association of Anatomical and Functional Brain Properties with Outcomes: Figure 3 shows lesion data from 8 patients with left hemisphere strokes and aphasia who received 4 weeks of intensive therapy. We collected structural and rs-fMRI scans and behavioral assessments before and after treatment. We utilized a variety of brain imaging metrics to investigate the effects of baseline anatomical and functional brain properties on treatment outcome and delineate the brain functional reorganization in response to treatment. In this preliminary study we were able to identify specific rs-fMRI connectivity that influences language and spatial attention improvements following treatment.

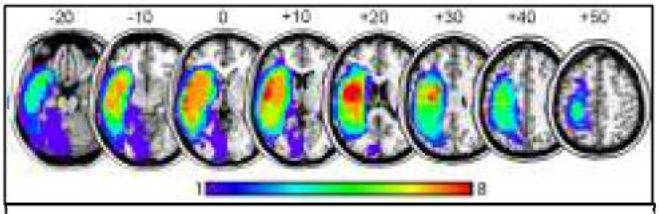


Figure 3. Topography of Stroke. Lesion overlay map in atlas space. Color scale: number of subjects with lesions at each voxel

Behavior Changes during Therapy: A battery of clinically-relevant and standard tests were used to assess language and attention abilities. Overall, patients achieved significant improvements across most language and attentional domains: Boston Naming Test (BNT), Aphasia Quotient (AQ), WAB-R Repetition (Rep), Raven's Progressive Matrixes (RAV) and Connor's Continuous Performance Test (CPT-2) showed significant changes following treatment ($p < 0.05$), while changes in WAB-R Reading and Writing scores suggested trends ($p = 0.116$ and $p = 0.073$, respectively). Principal component analysis revealed that behavioral measures at baseline formed two factors that explained 85% of the variance. The first factor, labelled AQ, comprised all language related processes including the BNT, AQ, Rep, Reading and Writing. The second factor included only the CPT II score (Figure 4a). Similar to visit 1 scores, behavioral data following treatment loaded on the two factors and explained 88% of the variance (Figure 4b). These results suggest that a common central mechanism underlying language-related performance is probably independent from the mechanism involved in attention-related tasks.

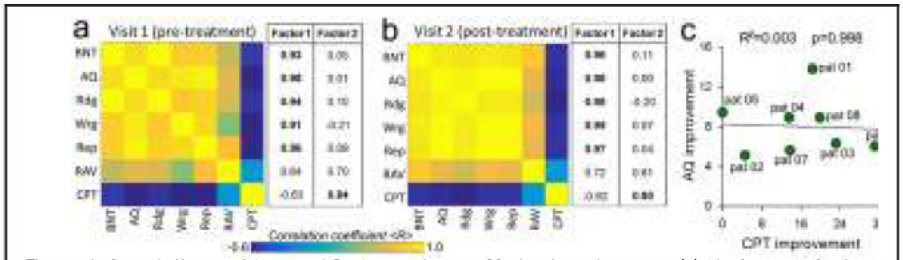


Figure 4. Correlation matrices and factor analyses of behavioural scores. (a) Heat map (left) shows the correlation across all behavioural scores at baseline (visit 1). Table (right) shows principle component analysis. Two main factors were identified, factor 1 contained all language domains, AQ, while factor 2 contained CPT. RAV loaded equally on both factors. **(b)** Behaviour scores after therapy (visit 2) shows similar associations to baseline. **(c)** Scatter plot shows the correlation between behaviour changes in AQ (factor 1) and CPT (factor 2). Despite both behavioural measures showing significant improvement, there were no correlation between them. Higher scores indicate better improvement.

Relationship between brain properties and behavioral changes. We investigated the extent to which anatomical and functional brain properties at baseline predict treatment gains using a correlational model. Lesion size was not related to AQ (r=0.23, NS) or CPT-2 gains (r = -0.11, NS). We also investigated the relationship between lesion location and outcome using a voxel-wise logistic regression.[120] There was no correlation between lesion location and outcome. However, we observed that AQ changes were associated primarily with a cluster in the left temporal lobe, while CPT-2 changes were associated with lesions in the frontal cortex and superior parietal lobes. A larger sample will allow us to evaluate these associations in greater detail.

We also used advanced graph theoretical analysis to characterize global and local brain properties during rs-fMRI.[121,122] First, we generated brain graphs using functional connectivity estimated between each pair of the 264 functional brain regions.[123,124] Then, we computed global and local functional properties of individual brain graphs using the brain connectivity toolbox (https://sites.google.com/site/bctnet/). Global network properties included clustering (information segregation), global efficiency (information integration), and modularity (the near-decomposability of the network into a community structure of sparsely interconnected modules).[121] Efficiency at baseline was associated with AQ ($p<0.05$), but not CPT ($p=0.23$) improvements. Modularity did not correlate with AQ ($p=0.13$) or CPT ($p=0.23$) changes after treatment. Finally, interhemispheric connectivity was only associated with CPT improvements ($p<0.05$). In addition to global properties, we examined whether functional connectivity between distinct brain networks (modules or communities) play a role in determining outcomes. Inter-modular connectivity for 5% density brain networks were generated by computing the total number of connections between any two modules and normalizing it by the total number of possible connections (Figure 5a). Association between modular connectivity and behavioral changes was assessed using a simple correlation analysis. We observed that AQ improvement showed a significant dependence on connectivity between the default-mode network and auditory regions (Figure 5b). CPT improvement showed a significant positive correlation with connectivity strength of the salience network and visual areas (Figure 5c).

These results show that improvement of aphasia symptoms following intensive therapy can be explained in part by baseline brain connectivity properties. Improvements across behavioral domains are dependent on global and system-specific connectivity.[125]

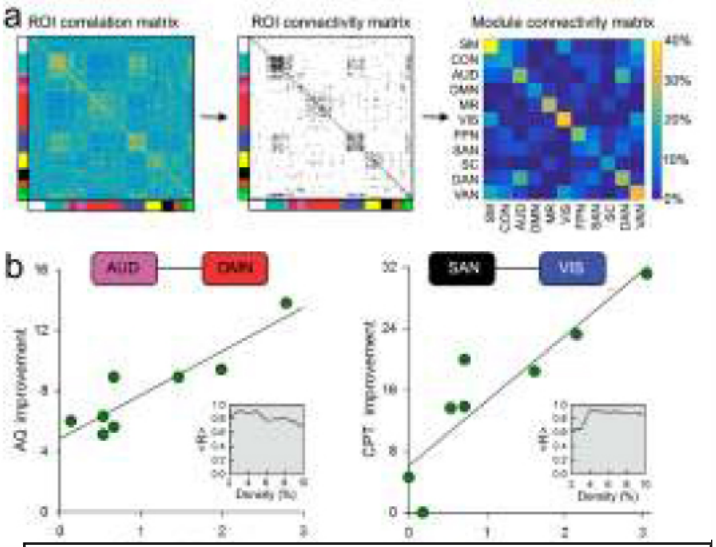


Figure 5. Treatment outcomes are driven by specific network connectivity (a) Modularity based connectivity maps were constructed by adding all ROI connections between any given pair of Modules and normalizing by the maximum number of connections. (b) Scatter plots show the modular connectivity (density = 5%) that was significantly ($p<0.05$, FDR corrected) related to treatment. Improvement in AQ scores was uniquely correlated to connectivity between default-mode network and auditory network, while improvement in CPT II was related to increased connectivity between SAN and visual network. Insets show the connectivity across all densities.

Instrumentation

Participants will complete assessments at specific time points from admission to the IRF to 18 months post-stroke. Table 3 lists study instruments by construct and indicates when participants will complete them.

We will ask patients to report **Demographic Characteristics**, then reconcile them with information in their medical records.

Clinical Characteristics, including stroke type, location, and volume, will be extracted from medical records. We will score the **Charlson Comorbidity Index** according to published criteria.[126] At each assessment time, we will collect information on current medications.

We selected 7 stroke-relevant **Neuro-QoL item** banks for CAT administration:[9,127,128] Fatigue, Sleep Disturbance, Depression, Cognitive Function, Communication, Satisfaction with Social Roles and Activities, and Ability to Participate in Social Roles and Activities. We will include one PROMIS item bank, Global Health, which measures overall physical and mental health.

The **National Institutes of Health Stroke Scale (NIHSS)** is a brief measure of neurological impairment.[129] It allows comparison of patients across settings and demonstrates excellent inter-rater reliability for acute stroke patients.[130,131] Baseline scores predict outcomes to 90 days.[132] The NIHSS demonstrates adequate to excellent concurrent validity with diffusion weighted MRI lesion volumes and perfusion-weight hypoperfusion volumes.[133] All persons performing NIHSS will be trained and certified.[134]

The **Apraxia of Speech Rating Scale (ASRS).**[135] We will distinguish between participants with apraxia of speech plus aphasia and those with aphasia alone using speech errors with words of increasing length and relative vowel duration in three-syllable words with weak-strong stress pattern (e.g., banana, potato).[136] Then,

for those with apraxia of speech plus aphasia, we will use the ASRS,[135] a valid 16-item rating scale, to quantify the presence or absence, relative frequency, and severity of characteristics associated with apraxia. The ASRS is scored during and/or after listening to the individual's speech during conversational speech, picture description, word and sentence repetition, and alternating and sequential diadochokinetic speech tasks.

Table 3. Study Instrumentation and Assessment Timing

Instrument	Time (min)	Construct	Mode	When
Demographic Characteristics				
Sociodemographic Information*	5	Various	Interview	A‡
Clinical Characteristics				
Stroke characteristics*	-	Person characteristics	Medical record review	A
CT/MRI review for lesion size and location	-	Brain structure	Medical record review	A
Charlson Comorbidity Index[126]	-	Body structure and function	Medical record review	A
Medication review	-	Various	Medical record review & patient reported	A D 6 12 18
Neuro-QoL Fatigue, Sleep Disturbance, Depression*	10	Fatigue, sleep, mood,	Patient-reported	A D 6 12 18
Apraxia of Speech Rating Scale[135]	10	Motor-speech planning	Performance test	A D 6 12 18
NIH Stroke Scale* (NIHSS)	10	Sensory, mental, movement-related & communication functions	Interview	A & D
Inpatient Rehabilitation Facility-Patient Assessment Inventory (IRF-PAI) (formerly the FIM™ Instrument)	-	Movement-related, self-care, mental functions	Medical record review	A W 6 12 18
Biomarkers				
Resting state brain fMRI (AbilityLab subsample, 100)	30	Network connectivity	Imaging	A
Genetic samples	5	DNA polymorphisms	Saliva sample	A
Aphasia Treatment				
Inpatient SLP Therapy	-	Current Procedural Terminology codes, therapy taxonomy	Medical, financial records; patient log	E 6 12 18
Outpatient community groups, Private pay therapy	-	CPT codes, therapy taxonomy	Medical, financial records; patient log	Weekly after discharge
Outcomes – Linguistic				
Western Aphasia Battery-Revised (WAB-R)	60	Aphasia severity and classification	Performance test	A D 6 12 18
Outcomes – Cognitive-Communicative				
Communication Participation Item Bank (CPIB)	10	Participation in life situations, control over participation	Patient-reported	A D 6 12 18
Connor's Continuous Performance test-3 (CPT-3)	15	Attention	Performance test	A D 6,12,18
Communication Confidence Rating Scale for Aphasia (CCRSA)	10	Communication confidence	Patient-reported	A D 6 12 18
Communication Effectiveness Index (CETI)	10	Communication in everyday environments	Caregiver-reported	A D 6 12 18
Neuro-QoL Cognitive Function*	5	Cognition	Patient-reported	A D 6 12 18
Outcomes – Health-Related QOL				
Stroke & Aphasia Quality of Life Scale-39 (SAQoL-39)	10	Stroke & aphasia-related QoL	Patient-reported	A D 6 12 18
Neuro-QoL Satisfaction with Social Roles & Activities, Ability to Participate in Social Roles & Activities*	15	Community, social and civic life	Patient-reported	A D 6 12 18
PROMIS Global Health	5	Global health	Patient-reported	A D 6 12 18
Global Rating of Change (GRC)	2	Patients' global perception of improvement	Patient-reported	D 6 12 18

* NINDS Common Data Elements, including SES, education, age, sex, race/ethnicity, handedness, stroke etiology, location, etc.
‡ A=admission, D=discharge, E=Every day, W=weekly, 6=6 months post-stroke, 12=12 months post-stroke, 18=18 months post-stroke

The **IRF Patient Assessment Instrument (IRF-PAI)** is required by Medicare for payment. Similar to the FIM™[137], it uses a 7-point rating scale. Nurses and therapists complete it routinely at IRF admission and discharge. Study sites will collect scores weekly. Subscores reliably measure self-care, mobility, communication, and cognition.[137]

The **Western Aphasia Battery-Revised (WAB-R)**[82] measures linguistic (reading, writing, auditory comprehension, naming) and non-linguistic skills (drawing, calculation, block design). It demonstrates excellent reliability and validity.[138-140] The Aphasia Quotient (AQ) provides a global measure of aphasia severity and serves as the primary linguistic outcome. The AQ characterizes 8 aphasia types and severity. The Language Quotient (LQ)

includes reading and writing skills. The Cognitive Quotient (CQ) measures aspects of cognitive behaviors including calculation, praxis, drawing and visual-spatial skills in addition to oral and written language.

The **Communicative Participation Item Bank (CPIB)**[141] (primary communicative outcome) is a 10-item, generic self-report short form measuring communicative participation. Developers used IRT methods with self-report data from 701 individuals with neurologic disorders and head and neck cancer. Evidence supports its validity for use with persons with aphasia.[142]

Connor's Continuous Performance Test-3[143] is a computerized assessment of attention, specifically inattentiveness, impulsivity, sustained attention, and vigilance. It is used widely with children and adults with ADHD and other neurological disorders.[144,145] It has been used to identify attention deficits in individuals with aphasia.[146]

The **Communication Confidence Rating Scale for Aphasia (CCRSA)**[1,2,147] is a 10-item self-report measure that assesses confidence in a variety of different situations and people. Rasch analysis demonstrated that it can distinguish three levels of confidence in tasks of varying difficulty and across severities of aphasia.[1,2]

The **Communicative Effectiveness Index (CETI)**[148] provides information about the functional significance of changes resulting from SLP treatment and consists of 16 items that assess social needs, life skills, basic needs, and health threats. Caregivers who have an opportunity to observe the individual with aphasia are respondents. It demonstrates evidence of reliability and reliability,[148] and it is sensitive to change in communication behaviors.

The **Stroke and Aphasia Quality of Life Scale-39** (SAQoL-39)[149] (primary health-related QoL outcome) is an adaptation of the Stroke Specific Quality of Life Scale[150] for persons with aphasia. It measures physical, psychosocial, communication QoL, and energy. Published reports describe use with stroke patients without aphasia[151] and proxy respondents; there are small to moderate differences between patient and proxy responses.[152] It has been translated widely.[153-158]

PROMIS Global Health provides a summary index of physical and mental health.[54] It includes 10 items selected from PROMIS item banks; it correlates highly with the EQ-5D, another widely used measure of QOL. These global health scales can be used to summarize physical and mental health.

Global Rating of Change (GRC). Patients will complete a global rating of change at 6, 12, and 18 months post-stroke to measure perceived improvement from baseline and from the previous time point. This method permits testing for change from baseline to 6, 12, and 18 months; 6 to 12 and 18 months, and from 12 to 18 months. We will use a GRC item with a stem of "How would you say your ability to communicate has changed since [prior time point]", and 5 response levels of -1=worse, 0=no change, 1=a little better, 2=much better, 3=very much better. We will calculate sensitivity and specificity of each response option to estimate the point of least misclassification, which will determine the threshold for minimal improvement.[159]

Single-Nucleotide Polymorphism Genotyping. We will investigate SNPs previously characterized in genes, including Brain Derived Neurotrophic Factor (BDNF), Apolipoprotein E (APOE), Insulin Growth Factor 1 (IGF1), Catechol-O-methyltransferase (COMT), Fibroblast Growth Factor 2 (FGF2), and Vascular Endothelial Growth Factor A (VEGF-A). These SNPs modulate neuroplasticity in stroke patients and affect post-stroke recovery (references in Table 4). We will use Oragene Discover OGR-600 saliva kits (DNA Genotek, Inc.) and extract DNA using the Gentra Puregene Buccal Cell Kit (Qiagen) to identify SNPs. We will test DNA quality and purity, including A260/A280 ratios and visualization on agarose gels. We will quantify DNA yield using an Eppendorf BioSpectrometer and store purified DNA in -80C freezers.

Table 4. SNP-Specific Assays

Gene/ Protein	SNP	Codon Change	Amino Acid Change	Life Technologies Assay ID
BDNF[160,161]	rs6265	ATG, GTG	M66V	C_11592758_10
BDNF[100]	rs11030119	Intronic (A/G)		C_31701027_10
BDNF[104]	rs10835210	Intronic (A/C)		C_1751795_10
APOE[162]	rs429358	CGC, TGC	R130C	C_3084793_20
APOE[162]	r7412	CGC, TGC	R176C	C_904973_10
IGF1[163]	rs7136446	Intronic (C/T)		C_2801095_10
IGF1[163]	rs9989002	Intronic (A/G)		C_29575558_10
COMT[163]	rs4680	ATG, GTG	M158V	C_25746809_50
FGF2[104]	rs308379	Intronic (A/T)		C_802931_10
VEGFA[104]	rs833069	Intronic (C/T)		C_11400863_20

We will use PCR-based TaqMan SNP Genotyping assays, also known as TaqMan Allelic Discrimination assays, to genotype SNPs.[164] These products use the 5´-endonuclease property of the DNA polymerase to amplify and detect specific SNP alleles in purified genomic DNA samples.[165] Each assay allows genotyping for a specific SNP. It requires forward and reverse PCR primers and two allele-specific TaqMan DNA probes labeled with fluorescent reporter dyes (FAM or VIC reporter molecules) that recognize and hybridize to the biallelic SNP inside the DNA region amplified by real-time PCR (Figure 6). Each biallelic SNP will be genotyped with TaqMan

Allelic Discrimination assays using the Assay-On-Demand service of Life Technologies (Thermo Fisher). Assays are available commercially and optimized by Life Technologies at Thermo Fisher. We will perform reactions in a 96-well format in a total volume of 5 UL containing 5 ng of purified DNA, 1× TaqMan assay, and 1× genotyping master mix (Thermo Scientific). Real-time PCR cycling will consist of initial denaturation for 15 minutes at 95°C, 40 cycles with denaturation of 15 seconds at 96°C, and annealing and extension for 60 seconds at 60°C. We will acquire signals using a C1000 Touch Thermal Cycler (Bio-Rad); results of the assay will be determined by CFX Manager software provided with the thermal cycler (Bio-Rad). We will confirm and test results for false positives using the independent statistical clustering method k-means.[166] We will analyze gene-gene interactions between SNPs that have been linked to neuroplasticity at the cellular and molecular level in post-stroke recovery, including growth factors mediating neurogenesis, angiogenesis, synaptic remodeling and neuroprotection (see Table 4 for the specific polymorphisms). We will identify significant predictor models using multifactor-dimensionality reduction methods,[167 10] in which multi-dimensional genotypes are classified into high- and low-risk groups. An indicator for the high-risk group is defined in the first step. In the second step, the indicator variable for the high-risk group is considered a covariate, with other adjusted covariates in the regression model. Then, the significance of a gene-gene interaction is obtained by testing the indicator variable of the high-risk group.

Neuroimaging Data Collection and Analysis. AbilityLab patients will receive two rs-fMRI scans to estimate reliability, a high-resolution (1 mm) T1 anatomical scan, a T2 FLAIR axial scan, and two-shell DTI scanning method, which provides more precise estimates of Fractional Anisotropy (FA) and of probabilistic tractography. This protocol assures structural imaging will be available for all patients and functional connectivity imaging for 100 patients. We will complete brain-imaging analysis on free-share software including FIMRIB software library (FSL),[168] SPM,[169] FreeSurfer,[170] Caret,[171] and *ad hoc* routines written in Matlab, C++, Pearl, and Awk. We will use brain imaging data to quantify a number of measurements (Table 5) that will be used in Aim 2c. All anatomical and functional brain imaging data preprocessing and quality control will be performed using validated pipelines adapted from the Human Connectome Project.[172] High-resolution T1 images will be used to investigate global and local structural properties including global brain volume, voxel-wise based gray matter density and shape of cortical and subcortical structures, as well as lesion size (mm^3) and location. Global structural properties will be measured using SIENAX that estimates total brain tissue volume from a single image, normalized for skull size. It first strips non-brain tissue and uses the brain and skull images to estimate the scaling between the subject's image and standard space. It then runs automated tissue segmentation to estimate the volume of brain tissue and multiplies this value by the estimated scaling factor to reduce head-size variability between subjects. Regional gray matter properties will be assessed using the automated voxel based morphometry toolbox from FSL. This analysis includes brain extraction and segmentation, and non-linear registration to a standard gray matter template using FNIRT. We will take extra care during the registration steps to ensure minimal warping due to the presence of lesions. Lesion masks drawn on the high-resolution anatomical scans will be used as a mask to perform a Virtual Brain Transplant.[173] The T2 FLAIR scan will be used to quantify leukoaraiosis volume in patients using the FLAIR-histoseg method, that has been shown to be accurate and reproducible.[174] Functional brain properties will be assessed using rs-fMRI and graph theory analysis tools. Brain networks will be constructed and studied at multiple correlation thresholds and parcellation sizes. Nodes of the brain functional network will be defined using either a whole brain voxel-wise approach or various validated parcellation schemas ranging from 90 - 500 ROIs.[175] Since the value of the chosen threshold is important, we will test several threshold values, from a conservative threshold of 2% connection density (sparse networks) to a lenient threshold corresponding to 50% link density (dense networks). We will assess topological properties of the graphs using the open source brain connectivity toolbox (BCT, https://sites.google.com/a/brain-connectivity-toolbox.net/bct). Properties include clustering (a measure of information segregation), global efficiency (a measure of information integration), and modularity (a global measure of the near-decomposability of the network into a community structure of sparsely interconnected modules).[121,122] We will assess nodal properties of various regions of interest, in addition to global topological properties.

Table 5. Neuroimaging measurements

Outcome measures	Global	Local
Functional		
Functional connectivity in IFG and STG	√	√
Network properties (Clustering, efficiency and modularity)	√	√
Anatomical (gray matter)		
Lesion volume	√	
Lesion location		√
Gray matter density		√
Subcortical volume and shape		√
Gray matter micro-structural changes		√
Anatomical (white matter)		
Fractional anisotropy (FA)		√
Leukoaraiosis		√
Network properties (Clustering, efficiency and modularity)	√	√

We will use DTI to examine white matter property changes, specifically FA, which is sensitive to a range of pathologies using FMRIB's Diffusion Toolbox. We will correct DTI images for eddy currents that can cause stretches and shears in the diffusion-weighted images and head motion artifacts. A diffusion tensor model will be fitted at each voxel to determine voxel-wise FA, reflecting the degree of diffusion anisotropy within a voxel. Individual FA data will be realigned nonlinearly into a high-resolution common space (standard 1 mm). We will create and thin a group mean FA image to create a skeleton representing the centers of all tracts common to the group. Then, we will project individual FA images on this skeleton and compare it across individuals and conditions. We will perform probabilistic tractography using PROBTRACKX to generate a whole-brain tractography for each voxel or ROI. We will use pair-wise voxel connection strengths to construct whole brain or region-specific connectivity matrices. We will generate matrices from connection probabilities of voxels or ROIs and evaluate them using graph theory methods.

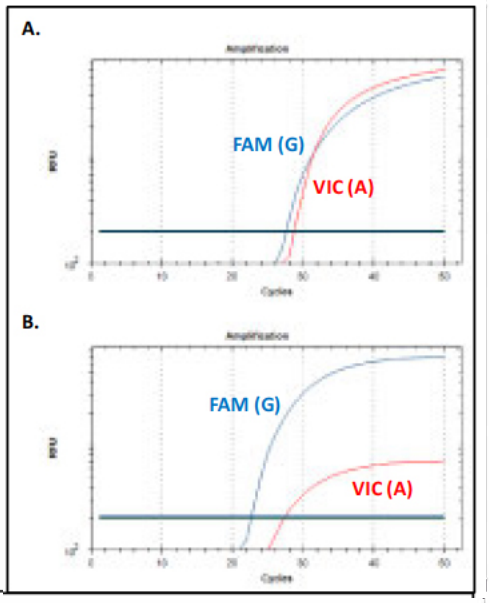


Figure 6. Allelic Discrimination Assays for COMT rs4680 polymorphism. FAM- and VIC-labeled probes specific for each allele, GTG and ATG respectively, are included in the PCR assay. A mismatch between probe and targeted DNA sequence reduces the efficiency of probe hybridization, DNA amplification and fluorescence detection. **A.** An equivalent increase in both FAM and VIC signals indicates that Patient A is heterozygote for rs4680 (GTG/ATG, or G/A). **B.** increase in FAM signal vs. VIC signal indicates that Patient B is homozygote for the FAM-based allele (GTG/GTG, or G/G).

Rehabilitation Therapy Services. We will use the information reported by IRFs to CMS on the Patient Assessment Instrument to characterize therapies. IRFs report total minutes of individual, group, and co-treatment therapy for SLP each week. We will train SLPs to use a log on their tablets during each therapy session to report the start and stop times of each treatment task and to indicate the language modality (auditory comprehension, oral expression, reading comprehension, written expression) that is the focus. SLP minutes and activities derived from therapist logs and notes will be used to summarize therapy for inpatient and outpatient settings. A survey of 56 SLPs across the 3 IRFs revealed that the SLPs were proficient at identifying the targeted treatment modalities. Extensive SLP training will be provided before and throughout the study to ensure accuracy. Ten percent of the treatment sessions will be video-recorded, so that the treatment logs can be checked for reliability. In addition, we will extract SLP therapists' progress notes and code details about therapy activities and patient participation. We will aggregate this information weekly throughout each patient's stay, guided by the rehabilitation therapy taxonomy work led by Whyte and colleagues.[103,173,174] After inpatient discharge, study participants or caregivers will complete a weekly checklist of outpatient therapies and other formal and informal rehabilitation services. A research assistant will call patients weekly during the first two months after discharge and then monthly to review and summarize the therapy and other service information.

Statistical Analysis

Sample Size Considerations. We base the sample size on the following considerations given the complex nature of the proposed longitudinal models that constitute the primary analyses. Although power analysis software is available for randomized mixed effects study designs,[176] no software is available for single group, observational mixed effects designs such as the proposed individual growth curve models. Simulation could offer an alternative approach to power estimation, but would rely on multiple assumptions about model parameters and variability. To our knowledge, preliminary data are not available to allow us to make such assumptions regarding long-term recovery of aphasia or QoL. Published models[3-5,8,111,113,177] use different outcomes and time points, and thus are insufficient for the model simulations required for this design. In general, samples larger than 500 are recommended for IGC models;[109] however, descriptive models have been reported for samples as small as 220.[4] Oberfeld and Franke[178] showed that generalized linear mixed models with repeated measures (i.e., SAS© PROC MIXED) control Type I error rates well under most conditions when the outcome is normally distributed and the sample size is 30 or larger. Thus, we propose a sample of 300 at 18 months, which allows confidence in robust trend analyses and sufficient power to develop viable models within the limits of the funding.

Based on our experience with stroke patients[10] we anticipate a 15% loss to follow-up at 6 months and an additional 10% loss at 18 months; thus, we will recruit 400 patients to retain 300 by the 18-month follow-up. Based on our experience, we expect to enroll 400 patients in approximately 30 months (Table 2). IGC models can accommodate missing data under the missing at random assumption, allowing participants with missing evaluation points to be retained in models. Thus, participants who miss an assessment time point but remain in the study for subsequent points are not lost; patient dropout is more of a concern for the missing at random assumption than for power. We will include all available longitudinal assessments for IGC modeling of all outcome measures to define post-stroke recovery trajectories.

Aim 1. Unconditional Model Determination: We will construct separate unconditional IGC models, with time as the only predictor, for each of the primary and secondary outcome measures (Table 3). Outcomes with ordinal scales may be transformed to interval measures, including the IRF-PAI subscales, using Rasch analysis.[179-181] For each outcome, we will determine whether recovery pattern over time is linear, curvilinear (quadratic or cubic polynomial), or non-linear (negative exponential, Figure 1). These models will include random subject intercept and slope, and the within-subject correlation between repeated measurements will be modeled using an appropriate variance structure (spatial correlation). Model fit will be assessed using residual plots and other diagnostic techniques, and the best-fitting model will be selected based on the Akaike and Bayesian information criteria. We will use PROC MIXED and PROC NLMIXED in SAS©. As a sensitivity analysis, we will also fit models treating time as a categorical variable to see whether the estimates are consistent with fitted models. These models will define the typical pattern of recovery in this patient population.

Aim 2. Conditional Model Determination**:** For each outcome, the selected unconditional model from Aim 1 will be expanded to include additional covariates (fixed effects). Based on the conceptual model Figure 2, these multivariable models will include time (and its appropriate functional form), and one of the following sets of covariates as described in Table 3: demographic characteristics (Aim 2a), clinical characteristics (Aim 2a); therapy characteristics (Aim 2b); and imaging biomarkers (including lesion size and location based on the multi-modal parcellation atlas of the human cortex,[182] and absolute values of network connectivity from imaging studies) or genetic markers from assays (Aim 2c). Model selection strategy will follow a purposeful model selection approach described by Hosmer and Lemeshow;[53] we will investigate clinically-relevant interactions and explore functional forms of continuous predictors. Model fit will be assessed using residual plot and other diagnostics methods.

Next, we will combine the variables from the selected multivariable models in each of the 4 groups (demographic + clinical, demographic + biomarkers, demographic + clinical + biomarkers, demographic + clinical + treatment, and demographic + clinical + biomarkers + treatment) to test the relationships in Figure 2, assess the additional effects of the variables in each conceptual group, and reduce to the most parsimonious model. We will use the final IGC models, after validation in Aim 3, to construct an interactive tool which clinicians can use to produce individual trajectories by specifying values for each patient, stroke, and therapy covariate.

The fitted models allow us to test Aim 1 and 2 hypotheses. For Aim 1, we expect curvilinear trajectories as the best-fit models for all outcomes, but that linguistic outcomes improve to plateau around 6 months post-stroke, whereas cognitive-communicative and QoL outcomes improve to plateau at around 18 months. We expect lesion size and initial aphasia severity (Aim 2a) and neuroplastic polymorphisms associations (Aim 2c) will have negative associations, and that CPT units (Aim 2b) and resting state connectivity (Aim 2c) will be positive.

Aim 3. Model Stability: Model validation requires an external sample, which is beyond the scope of this study. Thus, we will evaluate the stability of the final models selected in Aim 2 using bootstrap and cross-validation. Stability refers both to the variables included in the model and its predictive ability.[183] To evaluate variable selection, we will use bootstrap to resample cases B=500 times. First, we will fit each of the models from Aim 2 to the resampled data sets, and examine the bootstrap distribution of the estimated parameters and estimate the proportion of models in which each predictor was selected. Variables with low selection probabilities will be reconsidered for inclusion. Next, we will backward select each sample starting with the full model and will estimate the probability of selection for each variable. As in Altman and Andersen,[183] we will consider updating the final model by including variables with high probability of selection. To examine predictive validity, we will examine each model using Monte Carlo cross-validation with repeated random subsampling. We will split cases randomly into training and validation sets R=500 times, and fit the final model with the same set of predictors as selected in the final models in Aim 2 using the training sample in each split. We will use these training set parameter estimates to obtain fitted values for each subject in the validation set at the time points shown in Table 3. Because the outcome is a continuous variable in IGC models, we will use the median absolute deviation between the observed and predicted outcome at each time point as the measure of model performance. We will use the median absolute deviation distribution across the R splits to obtain confidence intervals. We will consider the model to have good predictive performance if the median absolute deviation is less than or equal to the MCID value estimated for the relevant time point for the instrument. The results of the bootstrap and cross-validation analyses will allow us to confirm the stability of the models selected in Aim 2, and to refine them if necessary.

Potential Problems, Alternative Strategies, and Benchmarks for Success. The project timeline provides benchmarks for project success. Potential problems involve slow participant accrual and high attrition. The recruitment and retention plan addresses these issues. We will extend accrual or add an additional site to assure we have a sample of 300 at 18 months, if needed. We have allowed sufficient time in the work plan for these possibilities. We will re-budget resources to meet slow accrual or low retention, if needed.

PHS Human Subjects and Clinical Trials Information

OMB Number: 0925-0001 and 0925-0002

Expiration Date: 03/31/2020

Are Human Subjects Involved	● Yes ○ No
Is the Project Exempt from Federal regulations?	○ Yes ● No
Exemption Number	❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8
Other Requested Information	

Human Subject Studies

Study#	Study Title	Clinical Trial?
1	Defining Trajectories of Linguistic, Cognitive-Communicative and Quality of Life Outcomes in Aphasia	No

Section 1 - Basic Information (Study 1)

1.1. Study Title *

Defining Trajectories of Linguistic, Cognitive-Communicative and Quality of Life Outcomes in Aphasia

1.2. Is this study exempt from Federal Regulations * ○ Yes ● No

1.3. Exemption Number ❑ 1 ❑ 2 ❑ 3 ❑ 4 ❑ 5 ❑ 6 ❑ 7 ❑ 8

1.4. Clinical Trial Questionnaire *

1.4.a. Does the study involve human participants?	● Yes	○ No
1.4.b. Are the participants prospectively assigned to an intervention?	○ Yes	● No
1.4.c. Is the study designed to evaluate the effect of the intervention on the participants?	○ Yes	● No
1.4.d. Is the effect that will be evaluated a health-related biomedical or behavioral outcome?	● Yes	○ No

1.5. Provide the ClinicalTrials.gov Identifier (e.g. NCT87654321) for this trial, if applicable

Section 2 - Study Population Characteristics (Study 1)

2.1. Conditions or Focus of Study

- This longitudinal cohort study evaluates linguistic, cognitive-communicative, and health-related quality of life (QoL) recovery in persons with stroke-related aphasia up to 18 months after onset.

2.2. Eligibility Criteria

We will enroll individuals with a primary diagnosis of stroke and aphasia on first admission to each of three Joint Commission-accredited IRFs: The Shirley Ryan AbilityLab, Alexian Brothers Rehabilitation Hospital (ABRH) in Elk Grove Village, Illinois, and Mary Free Bed Rehabilitation Hospital (MFBRH) in Grand Rapids, Michigan, for a total of 300. Inclusion criteria are a primary diagnosis of a first stroke with aphasia, age 21 years and older, first admission for inpatient rehabilitation, and sufficient cognitive capacity to provide informed consent and participate in testing.

2.3. Age Limits	Min Age: 21 Years	Max Age:
2.4. Inclusion of Women, Minorities, and Children	1254-HeinemannWomen.pdf	
2.5. Recruitment and Retention Plan	1255-CherneyRetention.pdf	
2.6. Recruitment Status	Not yet recruiting	
2.7. Study Timeline	1256-Heinemann Timeline.pdf	
2.8. Enrollment of First Subject	10/01/2019	Anticipated

Inclusion of Women and Minorities

The Shirley Ryan AbilityLab and the Alexian Brothers Rehabilitation Hospital are located in Cook County in the State of Illinois. The AbilityLab is located in the city of Chicago; Alexian is in Elk Grove Village in the northwest corner of the county. The AbilityLab attracts patients who are representative of the city of Chicago, whereas Alexian attracts patients more representative of the State of Illinois. The 2013 census estimates for the State of Illinois indicate a distribution by race of 77.7% White, 14.7% Black or African-American, 5.1% Asian, and the remainder composed of small percentages of other groups; 16.5% of the population was Hispanic (see http://www.lb7.uscourts.gov/documents/14c95482.pdf).

Cook County, which includes the city of Chicago, has the following census figures for 2013: 65.9% White, 24.6% African-American, 6.9% Asian, 1.8% two or more races and the remainder composed of small percentages of other groups; 24.7% of the population was Hispanic. Distribution by gender is 51.5% female and 48.5% male.

The 2013 census estimates for the State of Illinois indicate a distribution by race of 77.7% White, 14.7% Black or African-American, 5.1% Asian, and the remainder composed of small percentages of other groups; 16.5% of the population was Hispanic (see http://www.lb7.uscourts.gov/documents/14c95482.pdf).

FY 2016 admissions to all AbilityLab sites, including inpatient, outpatient, and day rehabilitation, were: White [redacted] African American [redacted] Asian [redacted] with the remainder composed of small percentages of other groups.a

- aAbilityLab served a[redacted]
- AbilityLab served a[redacted] population [redacted] The age distribution for all admissions was 0-44 years [redacted] 45-64 years [redacted] 65-74 years [redacted]; and 75+ years [redacted]

Mary Free Bed Rehabilitation Hospital is located in Grand Rapids, Michigan. The Grand Rapids, Michigan 2015 census estimates indicates a demographic distribution of 15.6% Hispanic (see https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?src=CF).

Of the non-Hispanic population, distribution by race was 59.0% White, 19.6% African-American, 1.9% Asian, and 3.9% more than one race. Distribution by gender was 51.1% female and 48.9% male.

For fiscal 2016, admissions to Mary Free Bed of patients with aphasia was [redacted] female and [redacted] male. The race distribution was [redacted] White; [redacted] African-American; [redacted] Asian; and [redacted] more than one race.

The attached planned Inclusion Enrollment Form represents the average demographic characteristics across the three participating Inpatient Rehabilitation Facilities. We will not exclude participants based on gender, race, or ethnicity. We expect to enroll slightly more women than men based on admissions and relevant census data.

In Illinois, the percentage of the population that is of Hispanic or Latino origin (of any race) is 16.5%; in Cook County it is 24.7%; in Grand Rapids, MI, it is 15.6%. Since we must require participants to be premorbidly literate in English, Latino-Americans may be under-represented compared to the national population.

The distribution of participants by minority status and gender may not exactly mirror the population statistics because the pool of available aphasic patients that receive services in the three Inpatient Rehabilitation Facilities is relatively small and may not be referred randomly from the population.

Inclusion of Children

The focus of this application is acquired aphasia in adults following stroke. Stroke in children is a rare event with a reported incidence of ischemic and hemorrhagic pediatric stroke ranging from 1.2 to 13 cases per 100,000 children under 18 years of age.[1] Language recovery takes a different form in children due to the increased plasticity of their central nervous system. Therefore, we will exclude children from the study.

1. Tsze DS, Valente JH. Pediatric stroke: a review. *Emerg Med Int*. 2011;2011:734506.

Recruitment and Retention Plan

Recruitment. Recruitment procedures that have been used successfully in previous research at each site will be utilized.

Stroke Patient Admissions with Aphasia at Participating IRFs and Likely Sample in Past 12 Months

Inpatient ‘Rehabilitation Facility	Admissions	Eligible	Likely to Consent
Shirley Ryan AbilityLab	[redacted]	[redacted]	[redacted]
Alexian Brothers Rehabilitation Hospital	[redacted]	[redacted]	[redacted]
Mary Free Bed Rehabilitation Hospital	[redacted]	[redacted]	[redacted]
Totals	[redacted]	[redacted]	[redacted]

We will enroll individuals with a primary diagnosis of stroke and aphasia on first admission from each of three Joint Commission-accredited IRFs: The Shirley Ryan AbilityLab, Alexian Brothers Rehabilitation Hospital in Elk Grove Village, Illinois, and Mary Free Bed Rehabilitation Hospital in Grand Rapids, Michigan, for a total of 300 patients followed to 18 months. Inclusion criteria are a primary diagnosis of a first stroke with aphasia, age 21 years and older, first admission for inpatient rehabilitation, and sufficient cognitive capacity to provide informed consent and participate in testing. The table shows the number of stroke admissions with aphasia over the past fiscal year. Based on our experience recruiting stroke inpatients for a Patient-Centered Outcomes Research Institute-funded study requiring patient self-report capacity, as well as the percentage of patients who are likely to consent to participate, we expect to complete enrollment within 30 months. We will over-recruit by 100 patients (400 consented patients), estimating 15% attrition by 6-months and another 10% attrition by 18-months, taking into account the likely mortality and morbidity.

Recruitment will be conducted by trained research assistants who are dedicated to the project at each site. The research assistants will review the stroke admissions on a daily basis to identify eligible participants. Physicians and speech-language pathologists at each site will be made fully aware of the study and will be notified if an eligible patient is admitted. They will inform their patients about the project and ask if a research assistant may contact them about the study. When patients agree, the research assistant will describe the purpose of the project and obtain informed consent from those who are willing to participate using an approved consent form and following IRB procedures. During the informed consent process, patients will be told about the purpose of the project, the procedures that we will use, the duration of the project, risks, benefits, alternative procedures, and information related to confidentiality. They will be told that participation is voluntary and that they can withdraw from the protocol at any time without prejudice concerning future services with the rehabilitation facility.

The research assistants will be trained in human subjects research and in the use of supported conversation techniques for persons with aphasia so they will be able to ensure understanding by the prospective subject. They will be trained and supervised by research speech-language pathologist Hurwitz, with oversight by co-PI Cherney.

Similar numbers of participants have been recruited successfully in past and current investigations at all project sites. Information about the project will be available on the respective project, laboratory, and center websites of each facility.

Based on stroke patient numbers at each study site, the likelihood of enrolling the projected number of participants is high. We will track recruitment status weekly to ensure that recruitment goals are met. In the unlikely event that these goals are not being met, we will consider adding a fourth site.

Retention. Numerous investigations have been conducted at each site that have often extended for many months. There have been few issues of losing participants to attrition due to the length of the protocol. The reasons for dropping out have included the following: death, illness, relocation, and family issues (e.g., death in family, new family responsibilities) rather than demands or duration of the research protocol.

We anticipate few drop-outs during the IRF stay, aside from medical complications that require transfer back to the acute care hospital. Depending on the cause of transfers, participants may be able to resume participation on readmission. They will be carefully screened to ensure that they still meet all eligibility requirements.

Following discharge from the IRF, a research assistant will call participants weekly during the first two months after discharge and then monthly to review and summarize the therapy and other service information. These phone calls also serve to promote retention. If needed, the frequency of the phone calls can be increased for individual participants to keep them connected to the study and study personnel.

In addition, participants will be assessed at 6, 12, and 18 months post-stroke with a variety of speech, language, cognitive-communicative, and quality of life assessments. Each of these visits will last approximately 3-4 hours and may be completed on consecutive days if necessary.

If needed, for the 6, 12 and 18 month follow-ups, participants may be seen in their homes. Some participants may not be able to drive and the use of public transportation could be challenging. We have found that conducting research visits in subjects' homes eases participant and family burden, increases attendance for scheduled sessions, and improves retention.

Reimbursement for participation will be provided which can facilitate retention. Participants will receive [redacted] after the inpatient rehabilitation discharge assessment. The honorarium will increase to [redacted] for the 6-month visit, [redacted] for the 12-month visit, and [redacted] for the 18-month follow-up. Subjects completing all assessments will receive a total of [redacted]. By reimbursing participation time for assessment sessions, we will be providing tangible acknowledgment that we value participant time. Increasing the amount reimbursed at each successive assessment will facilitate retention.

We have accounted for participants lost through attrition, by planning to recruit an additional 100 participants (i.e., 400) with the goal of 300 participants continuing through 18 months post stroke.

Project Timeline																							
Task	Description	Year 1				Year 2				Year 3				Year 4				Year 5			
		Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Aim 1: Establish a prospective cohort of stroke patients with aphasia, and define their typical patterns (trajectories) of linguistic, cognitive-communicative, and health-related QoL recovery																					
1.1	Obtain IRB approval at SRALab, ABRH, MFBRH, set-up REDCap database	■	■																		
1.2	Train research staff, orient therapists	■	■																		
1.3	Consent and complete inpatient/outpatient data collection			■	■	■	■	■	■	■	■	■									
1.4	Complete 6-month post stroke follow up assessments					■	■	■	■	■	■	■	■	■							
1.5	Complete 12-month post stroke follow up assessments							■	■	■	■	■	■	■	■	■					
1.5	Complete 18-month post stroke follow up assessments									■	■	■	■	■	■	■	■	■			
1.6	Request, extract, code therapy characteristics						■	■	■	■	■	■	■	■	■						
1.7	Data cleaning				■		■		■		■		■		■		■	■	■	■	■
1.8	Develop IGC models																■	■	■	■	■
1.9	Test H1																■	■	■	■	■
Aim 2. Identify factors that are associated with linguistic, cognitive-communicative, and health-related QoL outcomes from among: a) Patient factors, including demographic and clinical characteristics related to the stroke and aphasia; b) Treatment variables, including inpatient and outpatient aphasia therapy characteristics and other informal aphasia services; and c) Biomarkers, including genetic and neuroimaging biomarkers																					
2.1	Data cleaning				■		■		■		■		■		■		■				
2.2	Develop IGC models																■	■	■	■	■
2.4	Test H2a, b, c																■	■	■	■	■
Aim 3: Evaluate the stability of the linguistic, cognitive-communicative, and health-related QoL outcomes recovery models from Aim 2																					
3.1	Data cleaning				■		■		■		■		■		■		■				
3.2	Test H3 using bootstrap methods																■	■	■	■	■
3.3	Perform cross-validation																■	■	■	■	■
3.4	Disseminate findings						■								■			■	■	■	■

Inclusion Enrollment Reports

IER ID#	Enrollment Location Type	Enrollment Location
Study 1, IER 1	Domestic	The Shirley Ryan AbilityLab (SRALab) in Chicago, Illinois; Alexian Brothers Rehabilitation Hospital (ABRH) in Elk Grove Village, Illinois; and Mary Free Bed Rehabilitation Hospital (MFBRH) in Grand Rapids, Michigan.

Inclusion Enrollment Report 1

Using an Existing Dataset or Resource* : ● Yes ○ No

Enrollment Location Type* : ● Domestic ○ Foreign

Enrollment Country(ies): USA: UNITED STATES

Enrollment Location(s): The Shirley Ryan AbilityLab (SRALab) in Chicago, Illinois; Alexian Brothers Rehabilitation Hospital (ABRH) in Elk Grove Village, Illinois; and Mary Free Bed Rehabilitation Hospital (MFBRH) in Grand Rapids, Michigan.

Comments: Target enrollment is 300 participants, followed until 18 months post-onset. We will over-recruit by 100 patients (400 consented patients), estimating 15% attrition by 6-months and another 10% attrition by 18-months.

Planned

Racial Categories	Ethnic Categories				Total
	Not Hispanic or Latino		Hispanic or Latino		
	Female	Male	Female	Male	
American Indian/ Alaska Native	0	0	0	0	0
Asian	12	8	0	0	20
Native Hawaiian or Other Pacific Islander	0	0	0	0	0
Black or African American	33	27	0	0	60
White	142	118	33	27	320
More than One Race	0	0	0	0	0
Total	187	153	33	27	400

Cumulative (Actual)

Racial Categories	Ethnic Categories									Total
	Not Hispanic or Latino			Hispanic or Latino			Unknown/Not Reported Ethnicity			
	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	Female	Male	Unknown/ Not Reported	
American Indian/ Alaska Native	0	0	0	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0	0	0	0
White	0	0	0	0	0	0	0	0	0	0
More than One Race	0	0	0	0	0	0	0	0	0	0
Unknown or Not Reported	0	0	0	0	0	0	0	0	0	0
Total	0	0	0	0	0	0	0	0	0	0

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Section 3 - Protection and Monitoring Plans (Study 1)

3.1. Protection of Human Subjects	1257-Cherney_HumSub narrative 2017 FINAL 2July 2018.pdf
3.2. Is this a multi-site study that will use the same protocol to conduct non-exempt human subjects research at more than one domestic site?	● Yes ○ No ○ N/A
If yes, describe the single IRB plan	1258-Cherney_SingleIRB.pdf
3.3. Data and Safety Monitoring Plan	1259-Heinemann Cherney Data Safety Monitoring Plan.pdf
3.4. Will a Data and Safety Monitoring Board be appointed for this study?	○ Yes ● No
3.5. Overall structure of the study team	1260-Cherney_Study Team.pdf

Protection of Human Subjects

Risks to Human Subjects

a. Human Subjects Involvement and Characteristics: Four hundred participants with aphasia following stroke will be recruited upon admission to one of three inpatient rehabilitation facilities (IRF): the Shirley Ryan AbilityLab (SRALab) formerly the Rehabilitation Institute of Chicago, Alexian Brothers Rehabilitation Hospital (ABRH) in Elk Grove Village, Illinois, and Mary Free Bed Rehabilitation Hospital (MFBRH) in Grand Rapids, Michigan. Allowing for dropout, we anticipate that 300 subjects will complete all study procedures at 18 months post-stroke. All participants will undergo an initial screening that will include identification of demographic characteristics and medical history including CT/MRI review and medical complications. This review will be followed by a baseline assessment of speech, language, communication, and cognition skills as shown in the research plan. During the evaluation, subjects will be asked to complete routine speech-language tests such as name pictures, read words and sentences, describe a picture, repeat sentences, repeat sounds, and participate in a conversation. Specific tests include the NIH Stroke Scale, the Western Aphasia Battery-Revised, and the Connors Continuous Performance Test – 3. These tests will be administered at admission and/or just before discharge from the IRF. Participants will complete questionnaires about their perceptions and feelings regarding their general health, fatigue, sleep, mood, and communication abilities just before discharge. Their caregivers will also be asked to complete a questionnaire to rate communication skills in everyday situations.

We will ask subjects to provide a saliva sample at the start of their IRF stay. DNA will be extracted from the saliva sample and various single-nucleotide polymorphisms (SNPs) for BDNF, APOE, IGF1, COMT, FGF2, and VEGFA will be investigated. Subjects who are at the SRALab and who meet the eligibility requirements for MRI, will receive a resting state fMRI and a high resolution anatomical scan. At ABRH and MFBRH, we will review their clinical MRI scans to determine the size and anatomical site of lesions.

During the IRF stay, the IRF Patient Assessment Instrument which includes the Functional Independence Measure (FIM™) instrument will be administered as part of routine clinical care at admission and weekly thereafter. We will extract IRF-PAI scores from medical records. Information about speech and language therapy sessions also will be extracted from medical records, including frequency and duration of treatment. In addition, the speech-language therapists will complete logs on their tablets during each therapy session to indicate the start and stop times of each treatment task and to indicate the language modality (auditory comprehension, oral expression, reading comprehension, written expression) on which the task focuses. These logs will be analyzed for information regarding type of speech and language therapy services.

Following discharge from the IRF, participants are likely to seek other services such as outpatient therapy at hospitals and private or university clinics, aphasia conversation groups, and intensive comprehensive aphasia programs. Study participants and/or caregivers will complete a weekly checklist of these formal and informal rehabilitation services. A research assistant will call participants weekly during the first two months after discharge and then monthly to review and summarize the therapy and other service information.

Participants will be repeat assessments at 6, 12, and 18 months post-stroke with a variety of speech, language, cognitive-communicative, and quality of life assessments. Each of these visits will last approximately 3-4 hours and may be completed on consecutive days if necessary. The assessment will include the same tests that were administered at discharge from the IRF except for the NIH Stroke Scale.

Subjects will not be excluded on the basis of age, ethnic background, race, sex, or economic factors. However, since stroke is more prevalent in older individuals, the majority of the patients will be at least 50 years of age or older.

Inclusion criteria: Men or women with diagnosis of aphasia subsequent to a first left-hemisphere infarct(s) that is confirmed by CT scan or MRI; first IRF admission; at least 21 years of age.

Exclusion criteria: Any neurological condition other than cerebral vascular disease that could affect cognition or speech, such as Parkinson ’s disease, Alzheimer’s disease, traumatic brain injury, or the presence of right-hemisphere lesions.

Exclusion criteria for the rs-fMRI include (1) any metallic implants, tattoos on large body parts, claustrophobia, and (2) Pregnancy in women of child-bearing age.

The purpose of the study is to evaluate variables that affect recovery in aphasia such as aphasia type, severity, lesion size and location, selected genomic biomarkers, resting state fMRI, and amount, type and duration of

speech and language therapy and other services. These variables must be assessed with the person with aphasia.

All subject data will be securely maintained at each of the facilities as described below.

b. Sources of Materials: We will use existing patient records including MRI/CT scans to determine initial patient eligibility. We will evaluate subjects with the test battery for speech, language, communication, cognition and quality of life status at admission and discharge to the IRF, 6, 12 and 18 months post-stroke to obtain data on their deficits and changes that occur during recovery. We will obtain saliva samples on all subjects to evaluate selected polymorphisms biomarkers that affect neuroplasticity. We will conduct resting state fMRIs on a subset of subjects (those who are eligible for MRIs at the SRALab) and determine lesion size and site from clinical MRIs of other subjects. We will use existing patient records for IRF-PAI scores and to identify amount and duration of treatment during the IRF stay. We will obtain additional information about the type of speech and language therapy from logs that are completed by speech and language therapists. Participants will provide reports of their continued formal and informal speech and language services after discharge from the IRF. Data will be maintained in password-secured computer files and only personnel associated with the study will have access.

c. Potential Risks: Risks associated with the speech, language, and cognitive-communicative evaluations: These measures are routine and generally well-accepted by patients. The quality of life measures are also routine and will be administered with aphasia-friendly supports as needed. There are no more than the usual clinical risks associated with these activities such as fatigue or frustration while attempting tasks that are difficult.

Risks associated with the MRI: Only subjects who meet the MRI safety guidelines/eligibility criteria will receive r-s fMRIs. The main risk is one of discomfort since participants lie in a confined space with minimal head and body movements for about 30 minutes.

Another potential risk may be loss of confidentiality due to participation in the study.

Adequacy of Protection Against Risks

a. Recruitment and Informed Consent: Admission lists at AbilityLab, ABRH and MFBRH will be reviewed daily. Subjects with stroke and aphasia will be informed about the project by their physician or speech-language pathologist and asked if a research assistant may contact them about the study. If patients agree, the research assistant will describe the purpose of the project and obtain informed consent from those who are willing to participate using an approved consent form and following IRB procedures. During the informed consent process, subjects will be told about the purpose of the project, the procedures that we will use, the duration of the project, risks, benefits, alternative procedures, and information related to confidentiality. They will be told that participation is voluntary and that they can withdraw from the protocol at any time without prejudice concerning future services with the rehabilitation facility. The consenting process will be carried out by personnel who are trained in the use of supported conversation techniques to ensure understanding by the prospective subject. The IRB will review the project on an annual basis to ensure patient safety and confidentiality.

b. Protection against Risk: Participants will be offered frequent breaks between tasks to minimize risk of fatigue. The assessments can be administered over two test sessions on consecutive days if subjects are not able to tolerate the length of a single test session. Frustration with the evaluation tasks will be minimized by explaining the purpose of the tasks and providing frequent reinforcement for continuing to participate in them. To protect against fMRI risks, subjects will be carefully screened for MRI safety criteria by personnel who are thoroughly trained regarding safety procedures. These personnel will be trained in supported communication strategies for aphasia to ensure that subjects understand the safety criteria and to ensure good communication throughout the fMRI procedures.

To protect against any breach in confidentiality, data collected for this project will not be a part of medical records and will be maintained separately. Codes instead of names of subjects will be used on videotapes, data files, disks, and reports. Tapes, data files, and disks will be physically secured in locked areas and only authorized personnel will have access to them.

Potential Benefits to Human Subjects and Others

The risks are minimal and reasonable in relation to the anticipated future benefits. While there may not be any benefits to the subjects who participate in the study, the findings are likely to have important implications for individuals with aphasia in the future. It will provide information about factors that influence positive outcomes including the types of services that are beneficial. It will provide information about ways to measure patient-reported perceptions regarding progress during recovery and rehabilitation.

Importance of the Knowledge to be Gained

The knowledge gained will improve our understanding of the variables affecting recovery and rehabilitation process for individuals with aphasia such as aphasia type, severity, lesion size and location, selected genomic biomarkers, resting state fMRI, and amount, type and duration of speech and language treatment and other services. The data may lead to improved service delivery, reduced costs and effectiveness of speech-language services, thereby improving the communication skills and hence the quality of life of individuals with aphasia. Results may affect the field of neurorehabilitation since results may be applicable to other areas of deficit following stroke, and to other populations with communication problems requiring rehabilitation.

Data and Safety Monitoring Plan

A separate data and safety monitoring plan has been uploaded. We plan to have a Data Monitoring and Oversight Committee. All procedures will be carried out with approval of the Institutional Review Board of Northwestern University, which is the IRB for SRALab, and it will serve as the single site IRB.

Multi-Site Study Single IRB Plan

The Northwestern University Institutional Review Board (IRB) will serve as the Single IRB (sIRB) of record. The Northwestern University IRB is the IRB for the lead site, the Shirley Ryan AbilityLab, and is fully accredited by the Association for the Accreditation of Human Research Protection Programs, Inc. The utilization of a sIRB is in keeping with the NIH requirement that “all sites participating in multi-site studies involving non-exempt human subjects research funded by the National Institutes of Health (NIH) will use a single Institutional Review Board (sIRB) to conduct the ethical review required by the Department of Health and Human Services regulations for the Protection of Human Subjects at 45 CFR Part 46”.

The two collaborating sites (Alexian Brothers Rehabilitation Hospital in Elk Grove Village, Illinois, and Mary Free Bed Rehabilitation Hospital in Grand Rapids, Michigan, have agreed to rely on Northwestern University’s Institutional Review Board as the sIRB. If any sites are added after the award, they will rely on the sIRB.

All participating sites will, prior to initiating the study, sign an authorization/reliance agreement that will clarify the roles and responsibilities of the sIRB and participating sites.

Communication: As the lead team, the Shirley Ryan AbilityLab will be responsible for the initial submission to the sIRB as well as continuing review submissions. The lead team will serve as the primary liaison between the sIRB and collaborating study teams. Each participating site will be responsible for conveying all necessary information to the lead study team and will be responsible for completing all Human Research Protection Program requirements at their local institution. The Relying Human Research Protection Program will track the local study and manage all non-IRB requirements.

The Shirley Ryan AbilityLab and the Northwestern University IRB will maintain records of the authorization and reliance agreements and of the communication plan.

Data Safety Monitoring Plan

Overview

The proposed study is observational in which a cohort of 400 patients with stroke and aphasia are recruited on first admission to an Inpatient Rehabilitation Facility and followed up to 18 months after onset. Allowing for attrition, we anticipate a sample of 300 at 18 months. Participants will be recruited from three sites. There is no intervention and the risks are low. There are no more than the usual clinical risks associated with the speech, language, cognitive-communicative, and quality of life assessments such as fatigue or frustration while attempting tasks that are difficult. Risks associated with the r-s fMRIs are primarily related to physical discomfort as participants lie in a confined space with minimal head and body movements for about 30 minutes. There may be potential risks of loss of confidentiality due to participation in the study.

Data Monitoring and Oversight Committee (DMOC)

Based on NIDCD guidelines for observational studies, we will convene a DMOC to ensure patient safety and to ensure the validity and integrity of the data. DMOC membership will comprise individuals with the following qualifications:

- A physician with experience in stroke rehabilitation
- A research speech and language with experience in aphasia research
- A neuroscientist or neurologist with experience in neuroimaging, including resting state MRIs
- An epidemiologist with experience in health services research
- A neuroscientist or geneticist
- A person with aphasia and/or the family member of a person with aphasia

Potential conflicts of interest will be assessed and documented prior to appointment on the DMOC and annually thereafter. The DMOC will meet at the start of the study to review the study protocol and procedures including the Manual of Operations and its readiness for implementation. Thereafter, the DMOC will meet annually.

The DMOC will evaluate patient safety, determine participant burden, and provide advice on notification and referral of participants for any abnormal findings. Together with the Co-PIs and statistician, the DMOC will monitor overall study progress including recruitment and retention, adherence to study protocol, data quality control procedures and data quality. The DMOC will also review primary manuscripts and oral presentations that address the specific aims of the study.

Additional Plans

We plan procedures to ensure the quality and reproducibility of the collected data, including include training of the research assistants who will collect medical chart information and administer the speech, language, cognitive-communicative, and quality of life assessments. Co-PI Cherney, assisted by Research SLP Hurwitz, will provide initial training as well as continuous monitoring throughout the study. The project manager will receive weekly logs of the assessments that are scheduled and will assign 10% of them to be videotaped. Videos will be reviewed to ensure that the assessments are administered correctly; the assessments will be rescored by Research SLP Hurwitz to ensure that the test results are reliable. The research assistants will complete American Heart Association training and be certified to administer the NIH Stroke Scale. Research SLP Hurwitz has more than 10 years of experience serving as a blinded assessor for the many aphasia treat trials that Co-PI Cherney has conducted.

We will provide training and continuous monitoring to the clinical speech-language pathologists at each site who will be logging information about their treatment sessions with study participants. Training will include information about aphasia treatment in general, the rationale and purpose of the study, and the treatment logs they will complete with study participants. Feedback on videotaped aphasia treatment sessions will allow the clinicians to gain practice using the treatment templates. Training will continue until clinicians achieve more than 90% reliability logging the start and stop times of each treatment task, and identifying the language modality that is the focus of each task. We expect all clinicians to achieve this level of reliability. We surveyed SLPs at study sites; the majority were able to identify the treatment modalities accurately. However, for clinicians new to the site and for clinicians who require further practice, either their treatment sessions will be videotaped and coded later or the research assistant will observe treatment sessions and complete the logging until the clinician is able to demonstrate adequate reliability.

Co-PIs Heinemann and Cherney, together with statistician [redacted] will oversee the integrity and validity of the data that are entered into the REDCap database. All case report forms will be checked for completeness and entered into the database by the project manager. Ten percent of all case report forms will be rechecked by Research SLP Hurwitz or Co-PI Cherney. Based on their experience with aphasia and the outcome measures being used, they are able to recognize aberrant scores outside the range of responses typical of persons with varying types and severities of aphasia. One of the research assistants will double check data entry into the database from 10% of the case report forms.

Dr. [redacted] will supervise the master's level statistician who will be responsible for cleaning the data every other month during the data collection period.

The Study Team will also monitor safety. All team members will have completed IRB required training concerning reporting of adverse events. Any adverse event will be reported immediately by the team member who becomes aware of the event to the site PI, who will report the event to Co-PIs Heinemann and Cherney within 24 hours. They will report the event to the IRB within 48 hours of initial identification. All adverse events, even unrelated events, will be reported to the IRB. Unrelated events such as seizure, transient ischemic attack, and recurrent stroke are expected when conducting research with stroke survivors. We do not expect adverse events that are associated with the study procedures, but will continue to report all events, associated or not, to the IRB.

Study Team Structure

Data Collection Sites: 1) Shirley Ryan AbilityLab (Lead Site) – Chicago, IL, 2) Alexian Brothers Rehabilitation Hospital – Elk Grove Village, IL and 3) Mary Free Bed Rehabilitation Hospital – [redacted]

Co-PIs: Allen Heinemann, Leora Cherney (AbilityLab)

Co-Is: Allan Kozlowski (Mary Free Bed; Site PI; statistician), Linda Foster (Alexian; Site PI, Site manager), Marwan Baliki (AbilityLab, Brain Imaging), Andrea Domenighetti (AbilityLab; Genetics); [redacted] (AbilityLab & Northwestern University, biostatistician); Elliot Roth (AbilityLab; Physiatrist)

Project Manager: TBD

Research Speech-Language Pathologist (SLP): Rosalind Hurwitz (AbilityLab; provides training at all sites)

Site Manager: Roberta Virva (Mary Free Bed)

Research Assistants: TBD (AbilityLab), TBD (Alexian)*, TBD (Mary Free Bed)

AbilityLab Site – Lead Site

Administrative and Data Collection and Coordination Site

Team Members:

- L. Cherney – Study Co-PI
- A. Heinemann - Study Co-PI
- M. Baliki – Co-I, Brain Imaging
- A. Domenighetti – Co-I, Genetics
- R. Pichika –Research Associate Biologics Lab
- [redacted] – Co-I, biostatistician
- TBD – Master's level statistician
- R. Hurwitz – Research SLP
- TBD – Project Manager
- TBD - Research Assistant

Alexian Brothers Rehabilitation Hospital

Data Collection Site

Team Members:

- L. Foster – Site PI/Manager, Co-I
- TBD – Research Assistant *

Mary Free Bed Rehabilitation Hospital

Data Collection Site

Team Members:

- A. Kozlowski – Site PI, Co-I
- R. Virva – Site Manager
- J. Butzer – Research Administrator
- TBD - Research Assistant

*This research assistant will be hired by AbilityLab but will be located at ABRH

Drs. Heinemann and Cherney will meet at least monthly (via phone conference as needed) with the entire team. The project manager will meet weekly with the research SLP and research assistants from all sites. The PI and site PI's will have at least quarterly face-to-face meeting.

Dr. Heinemann will work closely with AbilityLab's research administration and the NIH project officer, obtain IRB approval, supervise chart extraction of therapy details, and oversee analytic and dissemination activities. Dr. Cherney will oversee training of all staff who interact with persons with aphasia including: informed consent; assessment of linguistic, cognitive-communicative, and quality of life; and weekly and/or monthly follow-up calls regarding formal and informal activities post-discharge from the IRF to 18 months post-stroke. She will oversee training of clinical speech-language pathologists at all sites in use of the treatment logs during their regular SLP sessions, oversee imaging and genomics activities, and assure data integrity. Together they will assure the quality of the research design and overall scientific conduct of the project.

Section 4 - Protocol Synopsis (Study 1)

4.1. Brief Summary

4.2. Study Design

4.2.a. Narrative Study Description

4.2.b. Primary Purpose

4.2.c. Interventions

Type	Name	Description

4.2.d. Study Phase

Is this an NIH-defined Phase III Clinical Trial? ❍ Yes ❍ No

4.2.e. Intervention Model

4.2.f. Masking ❍ Yes ❍ No

❑ Participant ❑ Care Provider ❑ Investigator ❑ Outcomes Assessor

4.2.g. Allocation

4.3. Outcome Measures

Type	Name	Time Frame	Brief Description

4.4. Statistical Design and Power

4.5. Subject Participation Duration

4.6. Will the study use an FDA-regulated intervention? ❍ Yes ❍ No

4.6.a. If yes, describe the availability of Investigational Product (IP) and Investigational New Drug (IND)/ Investigational Device Exemption (IDE) status

4.7. Dissemination Plan

Delayed Onset Studies

Delayed Onset Study#	Study Title	Anticipated Clinical Trial?	Justification
The form does not have any delayed onset studies			

Multiple PI Leadership Plan

Two Principal Investigators from the Shirley Ryan AbilityLab (formerly the Rehabilitation Institute of Chicago) are designated for this R01 application: Allen Heinemann, PhD, has expertise in health services and outcomes research and will serve as the contact PI; Leora Cherney, PhD, CCC-SLP will serve as the clinical and scientific expert in aphasia and speech-language pathology. Drs. Heinemann and Cherney have collaborated successfully on aphasia research for more than a decade and have coauthored two papers reporting the development of a communication confidence scale. Drs. Heinemann and Cherney have a combined 70-year history of successful grant management and demonstrated leadership in their respective roles, operating independently and collaboratively.

The proposed project will define the trajectories of linguistic, cognitive-communicative, and quality of life improvement during and after inpatient rehabilitation, identify the therapy characteristics associated with gains during and after inpatient rehabilitation, and assess objective measures of patient-reported QoL. Dr. Heinemann will work closely with AbilityLab's research administration and the NIH project officer, obtain IRB approval, supervise chart extraction of therapy details, and oversee analytic and dissemination activities. Dr. Cherney will oversee training of all staff who interact with persons with aphasia including: informed consent; assessment of linguistic, cognitive-communicative, and quality of life; and weekly and/or monthly follow-up calls regarding formal and informal activities post-discharge from the IRF to 18 months post-stroke. She will oversee training of clinical speech-language pathologists in use of the treatment logs, oversee imaging and genomics activities, and assure data integrity. Together they will assure the quality of the research design and overall scientific conduct of the project.

They will use a variety of mechanisms to assure regular communication between the PIs throughout the project. The PIs will conduct at least monthly (or more often as needed) meetings. Communication will not be limited to set meetings, but conducted when and as needed. AbilityLab provides abundant "huddle spaces" for informal and unscheduled meetings, and Drs. Heinemann and Cherney work in close proximity to each other, making such meetings easy to arrange.

The PIs have developed the proposal with the necessary care that should avoid future conflicts. However, should disagreements arise, the responsibilities are delineated clearly by the PI's respective areas of scientific and technical expertise. They report to AbilityLab's Chief Science Officer, Rick Lieber, who can mediate conflicts should they arise.

Dr. Heinemann is a Professor in the Department of Physical Medicine and Rehabilitation at Northwestern University's Feinberg School of Medicine and Director of the Center for Rehabilitation Outcomes Research at the AbilityLab. He has over 35 years of research experience in health services research and has served as PI for large center grants and others involving multi-site data collection. He is a diplomate in Rehabilitation Psychology and a fellow of the American Congress of Rehabilitation Medicine and the American Psychological Association. He serves as co-Editor-in-Chief for the *Archives of Physical Medicine and Rehabilitation*, and is on the editorial boards of *Rehabilitation Psychology, Journal of Head Trauma Rehabilitation*, and several other journals. He is the author of more than 300 articles. He received the Distinguished Career Award from the Rehabilitation Psychology division of APA. Dr. Heinemann has the research, clinical, and administrative expertise to ensure the successful management of the clinical and scientific aspects of this R01 grant.

Dr. Cherney is the Scientific Chair, Think and Speak Lab, at the Shirley Ryan AbilityLab and Professor in the Department of Physical Medicine and Rehabilitation and the Department of Communication Sciences and Disorders at Northwestern University. She has over 35 years' clinical experience in the field of speech-language pathology and is Board Certified by the Academy of Neurologic Communication Disorders and Sciences. She is the Founder and Director of the Center for Aphasia Research and Treatment at the Shirley Ryan AbilityLab. Her primary research interest is treatment efficacy for patients with aphasia, she serves or has served as Principal Investigator on several NIDILRR, and NIH-funded grants investigating novel treatment approaches, including the adjuvant roles of levodopa, cortical stimulation, and transcranial direct current stimulation in aphasia treatment. Dr. Cherney has the research, clinical, and administrative expertise to ensure the successful management of the clinical and scientific aspects of this R01 grant.

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Data Resource Sharing Plan

The proposed research will include data from 400 stroke patients with aphasia who are admitted to one of three inpatient rehabilitation facilities (IRFs) in the Midwest; we expect 300 patients to complete an 18-month, post-stroke follow-up assessment. The dataset will include demographic, behavioral and self-report data regarding linguistic, cognitive-communicative and quality of life status obtained during the inpatient stay and at 6, 12, and 18 months post-stroke. The dataset will also include information about therapy services including type, amount, and duration of treatment obtained during and after the inpatient stay. The dataset will include information about brain network connectivity derived from a resting state fMRI obtained at admission to the IRF and the presence or absence of specific genetic polymorphisms that have a role in neuroplasticity.

We will remove personal identifiers from the dataset before release for sharing.

We will make the REDCap data set available to users on request and only under a data-sharing agreement that includes (a) restrictions against efforts to identify study participants, (b) destruction of the data after analyses are completed, (c) reporting responsibilities, (d) restrictions on redistribution of the data to third parties, and (e) acknowledgement of the data source and funder.